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CONGENITAL DIAPHRAGMATIC HERNIA*

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BOSTON

THE problem of congenital diaphragmatic hernia in infancy is quite different from that of diaphragmatic hernia in later life. A review of the literature in 1931 by Hedblom[1] disclosed that 75 per cent of the patients with congenital diaphragmatic hernia died before the end of the first month of life. If this observation had excluded the cases of hernia through the esophageal opening, the mortality percentage would probably have been appreciably higher. In 1936, Orr and Neff[2] in a very extensive review of the literature could find but 17 cases of congenital diaphragmatic hernia that had been operated on in the first year of life, in which only 9 of the patients survived. In the Children's Hospital there have been 25 of these cases: in 9 of the earlier ones the policy of delaying operative interference until the child grew older was adopted. Of these 9 patients, 5 are known to be dead, 3 cannot be traced, and only 1 — who had a hernia through the esophageal opening — is known to be living. From these statements it must be apparent that there is little to recommend delayed or nonoperative treatment of diaphragmatic hernia in early life.

The situations in the diaphragm where congenital hernia occurs are the left and right sides posteriorly, where the defect is due to a persistent pleuroperitoneal canal (the foramen of Bochdalek), the esophageal opening, or the substernal opening commonly referred to as the foramen of Morgagni. Of these hernias, that occurring in a persistent pleuroperitoneal canal is by far the commonest. The fact that the hernia through the esophageal hiatus is commonest in adult life is due to the high mortality in infancy of patients with a hernia through the pleuroperitoneal canal.

The symptoms of diaphragmatic hernia may be respiratory, circulatory, digestive or a combination of all three, depending on the number of abdominal viscera in the thorax and on the size of the hernial ring. In a newborn infant showing cyanosis, dyspnea, or vomiting, diaphragmatic hernia is one of the conditions that should be considered. Cyanosis may be evident immediately after delivery. It may be transient and may appear only during nursing or crying, but in some cases it may be so severe that the constant use of an oxygen tent is necessary to sustain life. Vomiting may be only occasional or may follow most of the feedings. In patients surviving the neonatal period it is common to have poor weight gain or even weight loss.

Physical examination may show unduly rapid respiratory and pulse rates and a heart displaced away from the affected side. Percussion of the chest on the side of the hernia may be dull or tympanitic according to whether there is fluid or air in the misplaced viscera. Auscultation may reveal absent or distant breath sounds and possibly intestinal gurgles that, if present, at once suggest the correct diagnosis. When the major portion of the alimentary tract is in the thorax, tympany is lacking on abdominal percussion, and the abdomen is scaphoid in appearance.

Roentgenological examination should always supplement the history and physical examination. A roentgenogram without the use of contrast media will usually give all the necessary information and is probably safer than giving barium to the baby. If, however, a barium meal is required, only a thin mixture should be used, because there is real danger of causing obstruction or aspiration by giving too thick a mixture to small infants.

The normal findings in the chest are greatly distorted by x-ray examination. The affected side contains viscera that are continuous with those in the abdomen. The mediastinal structures, including the heart, are pushed to the opposite side, and both lungs may be greatly compressed.

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Treatment

There can be no question that surgical therapy is the proper treatment for these patients. There is sufficient evidence, from our experience and from the literature, to confirm the futility of expectant or medical measures. The general condition of the patient may be temporarily improved thereby; no enduring improvement can be expected, however, and the risks are great.

The policy of waiting until the child gets older and stronger is apparently responsible for the loss of a great many lives that might have been saved by a timely operation. On a theoretical basis, an operation performed in the first forty-eight hours of life is very advantageous. We have had an opportunity of doing this in two cases. Our experience has shown that infants in the first forty-eight hours of life stand major surgical procedures extremely well — in fact, far better than at the end of a week or ten days. Within the first two days one has the advantage of dealing with the intestine before it has become distended, and thus of being able to replace the intestines in the abdominal cavity — which might otherwise be impossible.

The preoperative treatment that we believe to be advantageous consists in making sure first that the infant is in a proper state of hydration, and secondly that the bowel is deflated as much as possible. The latter can be accomplished by enemas, by gastric suction and by placing the infant in a tent with a high concentration (90 to 95 per cent) of oxygen.

The anesthetic used in our recent cases was cyclopropane. This gives a maximum content of oxygen, slight positive pressure and good relaxation, all of which are important in these difficult cases. Its one drawback is, of course, its inflammability, but this risk is justified in view of the many

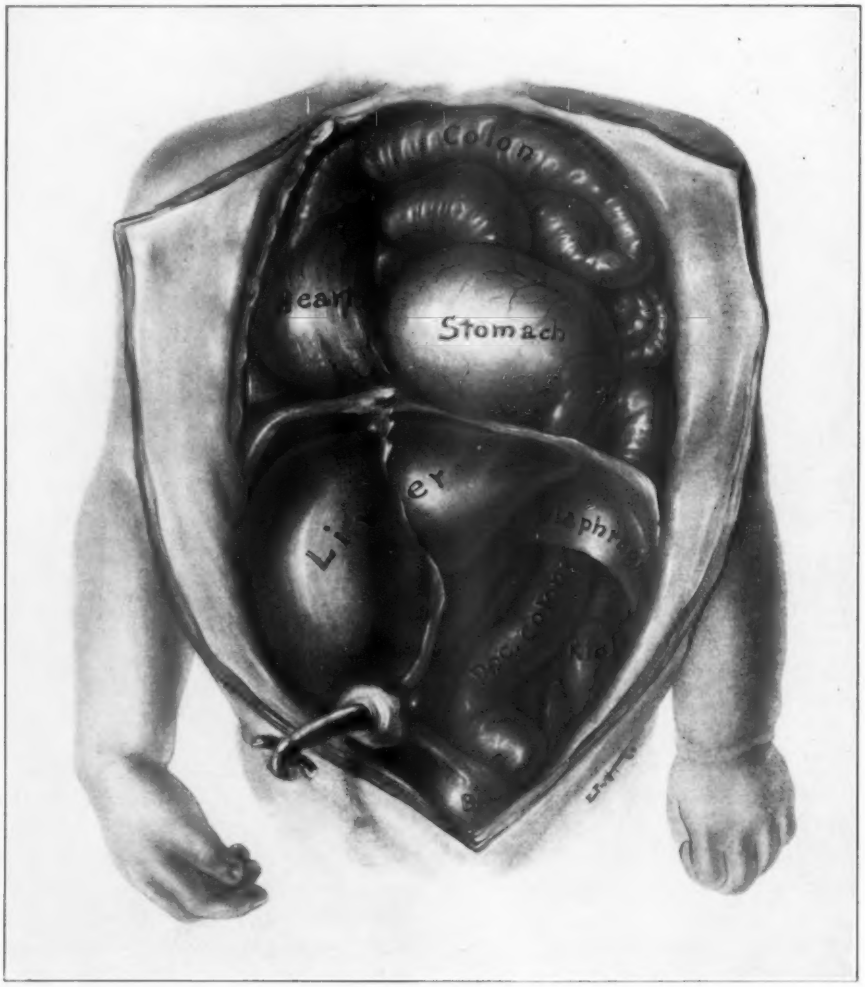


Figure 1.

Drawing made at post-mortem examination of a newborn baby with left-sided diaphragmatic hernia. The patient died in the fourth hour of life following severe cyanosis and respiratory distress.

advantages that it possesses. Whatever anesthetic is employed, there must always be provision for giving positive pressure if the need should arise.

It is our practice to paralyze the phrenic nerve, through a small supraclavicular incision, on the affected side before attempting repair of the hernia. The purpose of this procedure is to facilitate the closure of the hernial opening and to prevent excessive strain on the suture line during healing of the diaphragmatic wound. Immediately after this, one should proceed with the repair of the hernia. In one case we crushed the phrenic nerve at one

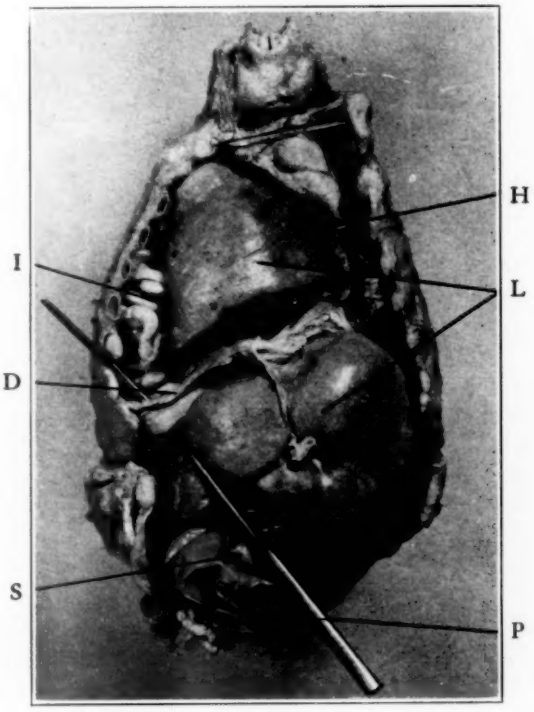


FIGURE 2.

Photograph of a post-mortem specimen showing a right-sided diaphragmatic hernia in a newborn child. The heart is displaced to the subject's left, and the left lung is greatly compressed. All the intestines are displaced up into the right pleural cavity. The liver has a deep fissure where it passes through the diaphragmatic opening. D = *diaphragm;* H = *heart;* I = *intestine;* L = *liver;* P = *probe passing through the diaphragmatic opening;* S = *stomach.*

operation, hoping to perform the hernial repair four or five days later, but the infant died before that time.

There seems to be a variance of opinion concerning the best surgical approach. We agree with Donovan[3] that the abdominal approach has many advantages for the infant, whereas this may not be true for the adult. In infants, the occurrence of adhesions between the intestines and pleural structures is extremely rare. In the absence of adhesions, it is much easier to pull the abdominal contents out of the chest from below than to push them out from above. In fact, in 4 of our cases it would have been impossible to reduce the hernia through a thoracic approach, because the abdominal cavity was too small to receive all the viscera.

The abdominal incision may be vertical through the rectus muscle of the affected side, or subcostal; either type gives a satisfactory approach. In each of our cases a rectus incision afforded an excellent exposure of the diaphragm. The hernial ring should then be stretched so as to allow air to enter the thorax. If an attempt is made to draw the intestines out of the chest before doing this, they are usually sucked back again as fast as they are pulled out; however, after some air has been allowed to enter the thorax, they can be readily withdrawn from the thorax and placed outside the abdominal wall, where they are wrapped in warm, moist gauze. If the hernial ring is small, the viscera must be withdrawn in a particular sequence: on the right side the liver must be reduced last, and on the left side, the spleen.

The next step in the operation consists in denuding the edge of the hernial ring of its serous membrane. The exposed muscle edges are then approximated with one row of mattress sutures of silk, followed by a row of interrupted sutures of the same material, to approximate the peritoneal edges. A small urethral catheter is led through the diaphragmatic wound into the pleural cavity. Just before the final diaphragmatic sutures are tightened, gentle suction is applied to the catheter, which is then withdrawn. In this way the lung can be quickly expanded.

The abdominal viscera are next replaced in the peritoneal cavity, and the abdominal wound is closed in layers if there is not too much tension. It must be remembered that in many cases the abdominal cavity has not developed because it never contained all its viscera, and hence there is not sufficient room to accommodate them. This seems to be an insuperable difficulty, but it can be met first by undercutting the skin to allow it to slide, and next by cutting across the rectus muscle to allow the abdominal wall to stretch. One then closes only the subcutaneous fascia with a running suture of silk and the skin with interrupted silk mattress stitches. This of course leaves an incisional hernia, which can be repaired later when the abdominal wall has become sufficiently stretched. The optimum time for this is five or six days after the first operation. This two-stage plan has several advantages over making a prolonged effort at a one-stage closure of the abdominal wall in the usual layers, if the latter must be done under great tension: it is far less shocking; it avoids plac-

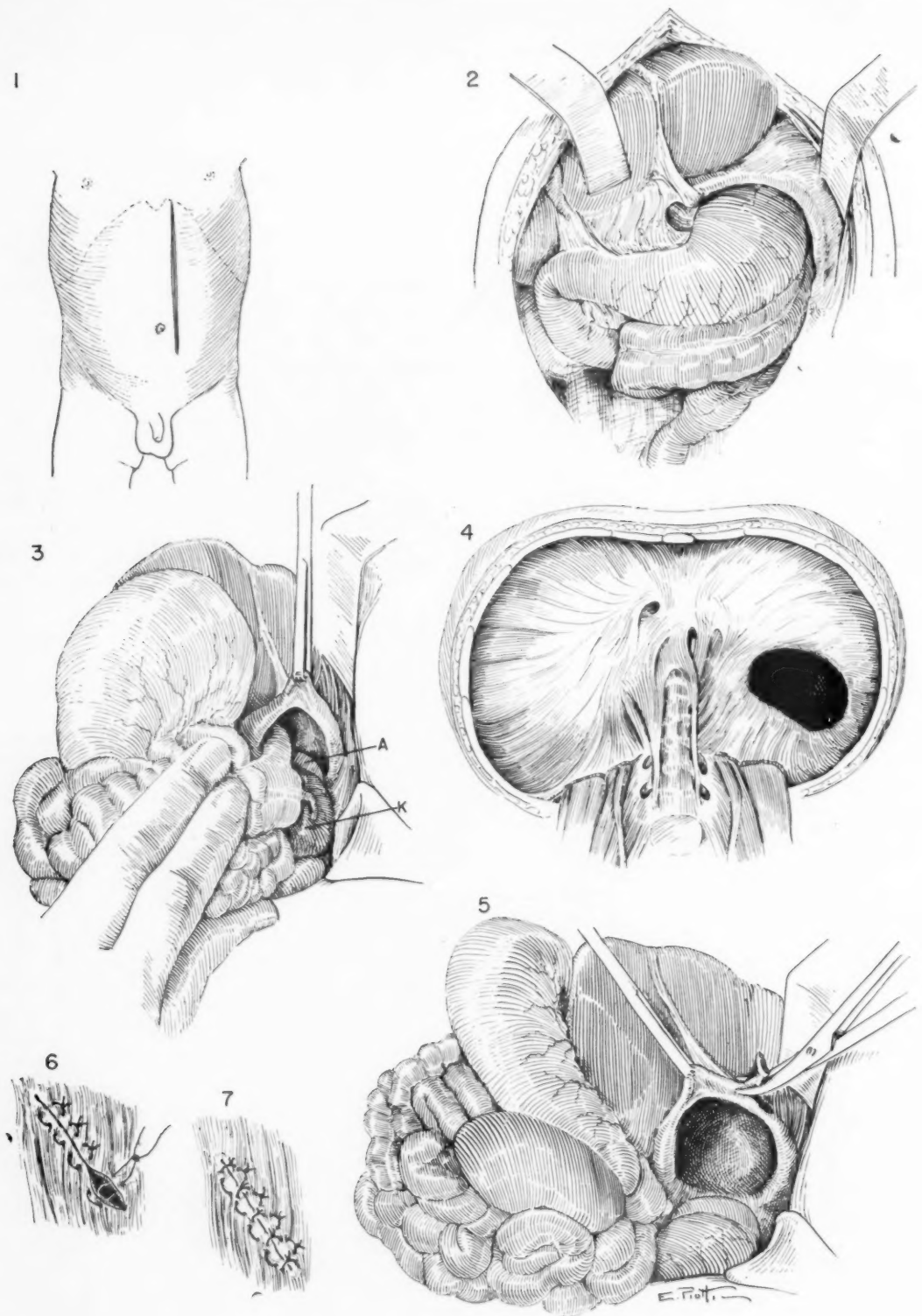
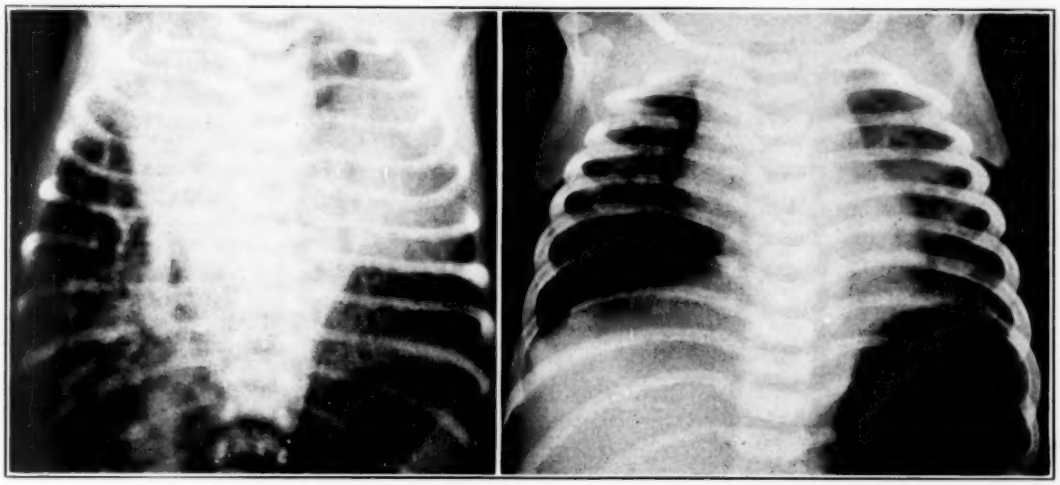


FIGURE 3.

Steps in the surgical repair of a left-sided diaphragmatic hernia of the type shown in Figure 1 and as exemplified in Cases 3, 5, 8 and 9. 1 = *position of the abdominal incision;* 2 = *view obtained on opening the abdomen (the stomach and colon are seen projecting up through the diaphragmatic defect; all the intestines, except the duodenum, are in the thorax);* 3 = *withdrawal of abdominal viscera from the chest;* 4 = *schematic view of under surface of diaphragm to show position of the opening in the left, posterolateral aspect of the diaphragm;* 5 = *cutting away rim of the hernial ring to make a raw edge;* 6 = *approximation of the diaphragmatic edges with interrupted mattress sutures of silk;* 7 = *reinforcement of peritoneal edges along the suture line with interrupted silk stitches;* A = *adrenal gland;* K = *kidney.*

ing great strain on the suture line in the diaphragm; and it avoids embarrassment of the respiratory and circulatory systems.

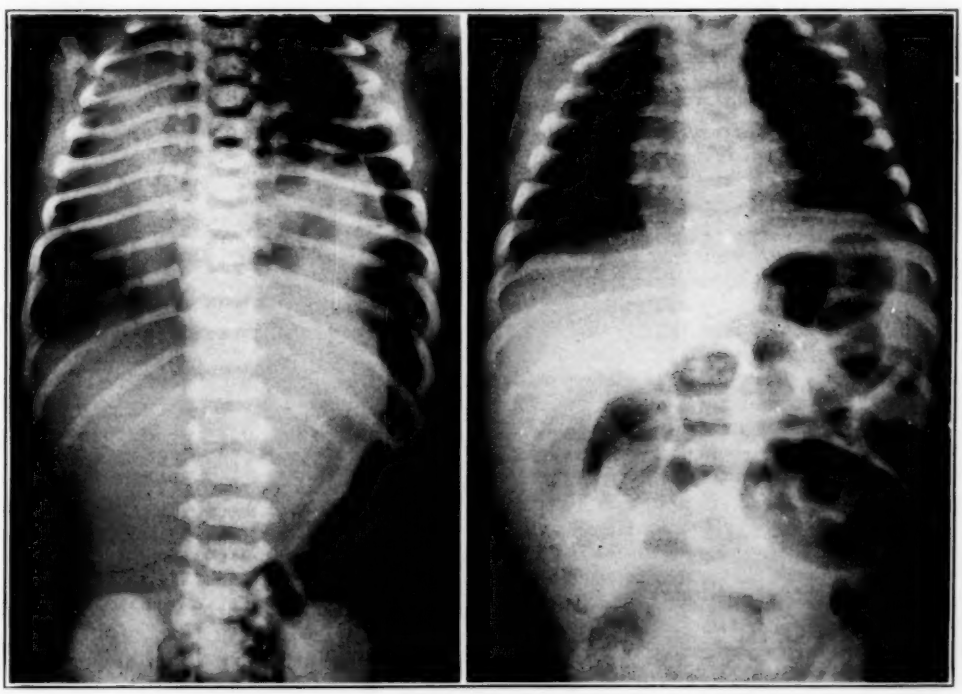
Closing the abdominal wall is by far the most difficult problem in the entire treatment of congenital diaphragmatic hernia. In our hands the anesthesia, the exposure of the diaphragmatic defect, — with an abdominal approach, — the reduction of the hernia, and the closure of the diaphragmatic openings have all been satisfactory, but the replacing and maintaining of viscera within the underdeveloped abdominal cavity still remained



A B

FIGURE 4. *Case 6.*

Roentgenograms of an eleven-day-old infant with right-sided hernia. A = *preoperative film;* B = *film taken three weeks after operation.*



A B

FIGURE 5. *Case 8.*

A = *roentgenograms of a thirty-six-hour-old baby with left-sided hernia. The gas-filled intestines are in the thorax, with the heart displaced to the right and the right lung compressed; operation was performed at forty hours of age.* B = *film taken at one month of age, showing normal expansion of the lungs and return of the heart to normal position.*

a problem until it was solved by the method of two-stage closure. In our early cases the abdominal wall was always completely closed in layers, in spite of the highly increased intraperitoneal pressure. This was probably one cause of the high mortality at that time.

The aftercare of these patients is important. They should be given a small blood transfusion at the end of the operation to replace any blood loss and to combat any hemorrhagic tendency of the newborn. The transfusion should be small enough to avoid any risk of embarrassing the right side of the heart, which in such cases is a very real danger. The infant is then placed in a tent with 90 to 95 per cent oxygen, for three reasons: first, to make breathing less labored; secondly, to keep the intestine deflated; and thirdly, to remove rapidly any room air which might have been trapped in the pleural cavity. Feeding is so regulated as to give an amount of fluid adequate to maintain water balance, but little attempt should be made to fulfill the caloric requirements for the first few days. If sufficient fluids cannot be given by mouth, they should be supplemented by parenteral fluids.

Case Reports

The brief summaries of 4 cases are as follows:

Case 2.* L. P., a girl, was born at full term and by a normal delivery. The birth weight was 7 pounds, 14 ounces. When feeding was attempted, the baby became cyanotic and choked. Vomiting often followed. This difficulty appeared to be more marked with breast than with artificial feeding. The patient was therefore removed from the breast and fed on a Lactogen formula. At that time a diaphragmatic hernia was suspected and confirmed by x-ray studies. For several weeks the baby continued to have cyanotic attacks when fed, and remained on the danger list at the maternity hospital. At the end of 3 months sufficient improvement had taken place for the patient to be discharged from that hospital. From that time until she was 2 years old and entered the Children's Hospital she had weathered attacks of measles, German measles and chicken pox, but had failed to gain weight satisfactorily. At 2 years she weighed 18 pounds, which is slightly under the normal weight for an infant of 1 year.

Physical examination showed an undernourished infant of good color. Percussion over the left chest posteriorly revealed dullness below the third rib and from the midline to the posterior axillary line. Anteriorly the percussion note was tympanitic. Breath sounds on the left were distant and only vaguely heard. The percussion note over the right chest was hyperresonant, but the breath sounds were normal and no rales were heard. The borders of the heart were difficult to define by percussion. The apex impulse could not be felt. The heart sounds were of normal rhythm but were distant. The abdomen was flat or perhaps a little scaphoid in appearance. The liver edge was 1.5 cm. below the costal border in the nipple line. The spleen was not palpable. No tenderness, muscular spasm or masses were felt.

Fluoroscopic examination showed the esophagus displaced slightly to the right. The barium entered the stomach without difficulty. The whole of the stomach was inverted within the thoracic cavity, with the greater curvature lying superiorly and the pylorus lying inferiorly. Six hours after administration, all the barium was in the colon. The cecum and ascending colon were in the left side of the chest, with the appendix visualized just lateral to the heart. The findings were those of a left-sided diaphragmatic hernia, with apparently a portion of diaphragm remaining anteriorly and posteriorly.

Under Avertin and novocain anesthesia a small transverse incision was made in the left side of the neck 2.5 cm. above the clavicle. The phrenic nerve was crushed with a small hemostat, and the wound closed. Four days after the preliminary operation, the abdomen was opened under Avertin and ether anesthesia. A left rectus incision was made extending from the costal border to a point 2.5 cm. below the umbilicus. An opening 7.5 cm. long and 5 cm. wide in the left side of the diaphragm extended from the nipple line toward but did not connect with the esophageal opening. Above the diaphragmatic opening were found the whole of the stomach, the spleen, the splenic flexure, half the transverse colon and 10 or 12 cm. of the descending colon. These organs were very easily delivered from the thoracic cavity, since there were only a few light adhesions around the cardiac end of the stomach. The abdominal viscera presented the not very uncommon condition of an unrotated colon with a rudimentary mesenteric attachment. There was no oblique attachment to the posterior abdominal wall of the mesentery of the small bowel, and only a small area of attachment of the hepatic flexure of the colon. The cecum and ascending colon were lying loose in the epigastrium just under the hernial opening. An incision was made around the edge of the hernial opening through both the peritoneal and pleural layers. As soon as the pleura was opened and air entered the thoracic cavity, the sac was delivered with no difficulty and was completely excised. Through the opening in the diaphragm the lung was seen to be collapsed, and the heart next to it in the same cavity without any pericardial covering. The ventricles stood out plainly. The auricles were not seen, and it is not certain whether there was not a rudimentary pericardium, as found in some of the published autopsies. The hernial opening in the diaphragm was closed with a row of interrupted sutures of silk to the pleural layer, a row of mattress sutures of silk to the musculature of the diaphragm and a row of interrupted silk sutures to the peritoneal layer of the sac. The abdomen was closed in layers without drainage.

The first 24 hours after operation were somewhat stormy. The temperature rose to 104°F., the pulse to 180, and the respirations to 60. The blood pressure was 70 systolic, and 20 diastolic. By the end of another 24 hours the temperature had dropped to 101°F., the pulse to 130 and the respirations to 25. During this period there was a left-sided pneumothorax, with a 90 per cent collapse of the left lung; there was no displacement of the heart. From this time on, the convalescence progressed satisfactorily and uninterruptedly. The patient was kept in the hospital longer than usual in order to make sure that there were no circulatory disturbances and that the lung was entirely expanded. She was discharged on the 26th day after operation. The wound was healed by first intention with a firm scar. The abdominal organs were in the abdominal cavity. The lung was completely expanded and there was no air or fluid in the pleural cavity.

The patient's general condition has been excellent since operation. She has gained weight, and has had no difficulty in breathing.

*This case, with a diaphragmatic hernia and absence of the pericardium, has been previously reported,[4] but because of its unusual interest a note is inserted concerning it.

CASE 5. K. C., a 6-week-old girl, entered the hospital on December 22, 1938, with a chief complaint of cyanosis since birth. At birth she weighed 6 pounds, 2 ounces. On the first day after delivery there were attacks of cyanosis and rapid breathing, particularly after the patient had been crying. It was found that these attacks could be controlled by placing her on her left side in an oxygen tent. Since that time cyanosis had appeared as often as three or four times a day, whereas on other occasions the color was normal for three or four days. The baby had taken its feedings well.

Physical examination showed that the thorax was symmetrical. The percussion note was resonant over the right side of the chest but dull over the left. The breath sounds were normal over the right lung but were completely absent over the left. Occasional gurgling sounds could be heard on auscultation over the left side. The respirations were rapid. The heart was displaced toward the right.

X-ray examination of the chest showed the entire left pleural cavity to be filled with loops of intestine, the left lung completely collapsed, the heart slightly displaced to the right and the right lung partially compressed.

Operation was performed on December 29, 1938, under drop ether anesthesia. A transverse incision was made in the neck above the left clavicle, and the phrenic nerve was crushed. The abdomen was opened through a left-rectus incision, splitting the muscle from the costal margin almost to the pubis. The defect was found in the posterolateral portion of the diaphragm. The entire ileum, all the colon except the descending portion, and the spleen were in the left pleural cavity. These viscera were withdrawn through the diaphragmatic opening and pulled downward, some of them protruding through the abdominal wound. The edges of the diaphragmatic opening were freshened and sutured with mattress stitches of silk, supplemented by a continuous silk suture to the peritoneum. The abdominal wall was closed with some difficulty, owing to tension. The peritoneum and posterior rectus fascia could be approximated, although there was some tearing of these structures during the placement of the stitches. The anterior rectus fascia was brought together with interrupted silk sutures, and the skin was closed with stitches of interrupted silk.

The patient was given parenteral fluids and was kept in an oxygen tent for 3 days. The temperature rose to a peak of 102.4°F. on the first postoperative day, but subsided to normal by the third day. The pulse rose to a peak of 160 and the respirations rose to as high as 70 on the 2nd postoperative day, but both subsided to normal by the 5th day. There was no vomiting or distention. Feedings were begun after the 3rd day. The wound healed well, and the patient was discharged home on the 29th day.

X-ray films of the chest on the afternoon of operation showed an extensive pneumothorax on the left, with displacement of the heart and mediastinum to the right. The left lung was completely collapsed. No abdominal viscera were seen in the chest. The left lung spontaneously expanded and by the 10th postoperative day completely filled the left chest. A barium examination of the intestinal tract on the 19th day showed a slight deviation of the lower end of the esophagus to the right at the point of its passage through the diaphragm, but there was no other evident abnormality. A film taken on May 6, 1939, showed the chest to be normal and the left diaphragm in the normal position.

The patient was last seen in December, 1939, at which time she was in excellent general physical condition.

CASE 6. J. M., an 11-day-old boy, entered the hospital on February 12, 1939, for treatment of a diaphragmatic hernia. The labor had lasted 15 hours. During the delivery the mother's condition was good, but the fetal condition was said to be poor. The baby was cyanotic at birth but was resuscitated with oxygen. The birth weight was 5 pounds, 12 ounces. His respirations were shallow and rapid, cyanosis continued, and he was limp. He had to be kept continually in an oxygen tent during this 11-day stay at the maternity hospital. The cyanosis became severe, and the patient's condition critical if he was removed from the tent for more than a minute or two.

Inasmuch as the breath sounds were diminished over the entire chest, it was thought that there was a massive atelectasis of the lung. Because of generalized twitching, a lumbar puncture was performed, which showed clear fluid. On the 5th day, x-ray examination of the chest showed evidence of diaphragmatic hernia.

Physical examination was only cursory because of the critical condition of the patient, who was ashen gray. He had to be kept in an oxygen tent during the greater part of the examination. The respirations were shallow and were 87 per minute. The pulse was poor, and the patient appeared to be in a state of shock. There was occasional vomiting of small amounts of bile-stained fluid. Breath sounds were normal over the left chest, but were absent over the right. Peristaltic sounds could be heard over the right side of the thoracic cage.

X-ray examination of the chest showed the entire right pleural cavity to be filled with abdominal viscera and the right lung completely collapsed. The heart was displaced to the left, and the left lung was compressed.

Operation was performed on February 14 under cyclopropane anesthesia. The right phrenic nerve was exposed above the clavicle and was crushed. The abdomen was opened with a right-rectus muscle-splitting incision running from the costal margin well down in the lower quadrant. There was a large defect in the posterior portion of the right diaphragm. Herniated into the right pleural cavity were a large right lobe of the liver, all the colon except the descending and the left half of the transverse portions, the distal half of the stomach and all the small intestine. Between the right and left halves of the liver there was a deep cleft into which the medial margin of the diaphragm fitted. The only way in which the contents of the right pleural cavity could be delivered was by first withdrawing the entire small intestine, then the large intestine and finally the right lobe of the liver. These viscera were displaced downward and to the left, and the intestines were allowed to protrude through the abdominal wound. The edges of the diaphragmatic opening were freshened and brought together with interrupted mattress sutures of silk. The right lobe of the liver was then allowed to fall back against this line of sutures so as to buttress the diaphragm repair. It was found impossible to replace the intestines in the abdominal cavity, and to close the abdominal wound. Transverse incisions were made in each rectus muscle, beginning from within the abdomen and cutting through all structures out to the subcutaneous tissues. This permitted closure of the subcutaneous fascia and skin of the abdominal wound. At the end of the procedure the patient's pulse and respirations were quite weak. He was given coramine and placed in an oxygen tent. His condition improved after a transfusion.

For 3 days after operation the patient was supported with parenteral fluids and was kept constantly in an oxygen tent. On the 1st postoperative day air was aspirated by inserting a needle into the right pleural cavity. There was no evidence of obstruction at any time. The skin sutures were removed on the 10th postoperative day. The patient's condition gradually improved so that he was discharged home at the end of 6 weeks.

X-ray examination on the afternoon of the operative day showed a pneumothorax on the right side and complete collapse of the lung. Subsequent films showed a gradual expansion of the lung, which was due to spontaneous absorption of air augmented by aspiration, and in about 10 days the right lung had completely filled its pleural cavity. Examinations of the gastrointestinal tract with barium 1 month after operation showed a normal stomach and intestines and no evidence of abdominal viscera in the thoracic cavity.

The patient was brought back to the hospital on June 24, at which time the incisional hernia of the abdominal wall was repaired. There was a satisfactory convalescence from this operation. When last seen, in December, 1939, the patient was very healthy, fat and well developed. He weighed 19 pounds and was in excellent general physical condition.

TABLE 1. *Data from Successfully Treated Cases of Diaphragmatic Hernia.*

CASE NO.	HOSPITAL NO.	AGE	SEX	SITE OF HERNIA	MAJOR SYMPTOMS	OPERATIONS*	ANESTHESIA	RESULT
1	141149	4 wk.	F	Esophageal	Vomiting, cyanosis	Diaphragm repair	Ether	Slight recurrence; symptomatic cure.
2	192085	2 yr.	F	Left pleuro-peritoneal	Vomiting, cyanosis	Phrenic crush, diaphragm repair	Ether	Cure
3	199566	3 wk.	M	Left pleuro-peritoneal	Cyanosis	Diaphragm repair	Ether	Cure
4	224541	9 mo.	M	Esophageal	Vomiting	Diaphragm repair	Cyclopropane	Symptomatic cure
5	228119	6 wk.	F	Left pleuro-peritoneal	Cyanosis	Phrenic crush, diaphragm repair	Ether	Cure
6	229511	11 days	M	Right pleuro-peritoneal	Extreme cyanosis requiring oxygen	Phrenic crush, diaphragm repair; abdominal repair 4 mo. later.	1st operation, cyclo-propane; 2nd, cyclopropane.	Cure
7	230878	18 mo.	M	Right pleuro-peritoneal	Vomiting, dyspnea	Phrenic crush, diaphragm repair	Cyclopropane	Cure
8	238818	40 hr.	M	Left pleuro-peritoneal	Cyanosis requiring oxygen	Phrenic crush, diaphragm repair; abdominal repair 8 days later.	1st operation, cyclopropane; 2nd, ether.	Cure
9	241377	48 hr.	M	Left pleuro-peritoneal	Cyanosis requiring oxygen	Phrenic crush, diaphragm repair; abdominal repair 4 days later.	1st operation, cyclopropane; 2nd, ether.	Cure

*A thoracic approach was employed in Case 4, an abdominal approach in all other cases.

CASE 8. D. C., a 36-hour-old boy, entered the hospital December 26, 1939, because of repeated attacks of cyanosis since birth. After delivery he breathed spontaneously, but the color was poor; oxygen was given immediately and was continued for 1½ hours. When removal from the oxygen tent was attempted, the color grew worse. During the first day and a half there was usually some degree of cyanosis, which could be temporarily improved when the child was placed back in an oxygen tent. No feedings had been given. There had been no vomiting.

At physical examination the respirations were rapid. There was moderate cyanosis. The chest was symmetrical. Respiratory excursions were more marked on the right than on the left. There were a normal percussion note and normal breath sounds over the right lung. There was hyperresonance of the left chest, but no breath sounds could be heard. Auscultation over the area of the left lung revealed occasional loud creaks and some faint gurgling sounds, suggesting the presence of intestinal loops in the left pleural cavity. The heart appeared to be displaced toward the right.

X-ray examination of the chest showed the left pleural cavity to be completely filled with loops of intestine, the left lung compressed so as to be unrecognizable in the film, the heart displaced partly to the right and the right lung partially compressed.

On December 27, when the baby was 40 hours old, operation was performed under cyclopropane anesthesia. The left phrenic nerve was exposed in the neck and was crushed. The abdomen was opened through a long left-rectus muscle-splitting incision running from the costal region well down into the left lower quadrant. Within the abdominal cavity were the distal third of the stomach and duodenum, the descending colon and the liver. Herniating into the left pleural cavity were the proximal two thirds of the stomach, the transverse and ascending colon, the jejunum, all the ileum and the spleen. The defect found in the posterolateral portion of the diaphragm was about 3 cm. long and 2 cm. wide. The abdominal viscera were readily withdrawn from the pleural cavity, no adhesions being encountered. The intestines were allowed to come out of the abdominal wound so as to give an adequate view of the under surface of the left diaphragm. The edges of the diaphragmatic opening were freshened, and the defect was easily closed with interrupted mattress sutures of silk, reinforced by a few interrupted silk stitches placed between the mattress sutures. On an attempt to force the intestines back into the abdominal cavity, it was found that the wound could not be closed in all its layers. It was impossible to approximate the peritoneum, the rectus muscle or the anterior rectus fascia. It was therefore decided to close only the subcutaneous fat and skin, which could be brought together rather easily. The subcutaneous fat was closed with a continuous silk suture, and the skin edges were approximated with end-on interrupted silk mattress stitches.

Following operation one transfusion of blood was given. The patient was placed in an oxygen tent. Respirations rose as high as 90 during the 1st postoperative day, but gradually fell to 40 by the 4th day. There was some fever for 3 days, after which the temperature remained normal. In order to avoid abdominal distention, the oral intake of fluid and milk was limited, and fluid requirements were fulfilled with the use of parenteral fluids and the administration of fluids by rectum. On the 7th day the skin sutures were removed and on the morning of the 8th day it was found that evisceration through the abdominal wound was beginning. Under drop ether narcosis the presenting loops of bowel were replaced in the abdominal cavity, and the abdominal wound closed with running catgut to the peritoneum and muscle in addition to through-and-through sutures of silk, including all layers except the peritoneum. It was striking to find that within

these 8 days since the first operation the abdominal wall had stretched sufficiently so that the wound edges could be readily approximated without tension.

Following the secondary repair the patient did well. There was no evidence of an incisional hernia, and the baby was discharged home in excellent condition on the 33rd day of life. In June, 1940, 6 months after operation, the baby was found to be in excellent health, above the normal weight for his age and having no respiratory or digestive difficulty, with the diaphragm in normal position, and with a firm abdominal scar and no hernia.

Since Orr and Neff's[2] collection from the literature of 9 cases of diaphragmatic hernia successfully operated on in the first year of life, we have found 8 more successful cases. Donovan[3] has been the largest contributor to these results, with 4 satisfactory cases. Three of these were cured, one after a secondary operation for recurrence, but the fourth patient had a slight recurrence without untoward symptoms. Sixteen patients with congenital diaphragmatic hernia have been operated on at the Children's Hospital since 1930. Nine of these have recovered, 7 of them being under one year of age (Table 1). The youngest patient was operated on when forty hours old. Of the 7 deaths, 1 occurred 5 days after a phrenicectomy before the herniorrhaphy was attempted, and 1 four days after operation, probably from pneumonia. The remaining 5 deaths were probably due to one or a combination of the following factors: failure to provide proper fluid balance, lack of positive-pressure anesthesia or too-tight closure of the abdominal wall.

Summary

The time to make the diagnosis of congenital diaphragmatic hernia is immediately after the baby is born. The time to attempt cure is within the first few days after birth or as soon thereafter as the patient can be taken to a hospital equipped to handle this type of case.

The policy of delaying operation until the infant is older is a hazardous one, and has been responsible for many deaths in the past.

One of the greatest problems of operating on these patients in early infancy has been that of finding sufficient room in the underdeveloped peritoneal cavity to receive the abdominal viscera. This problem has now been solved by the procedure here reported of closing only the abdominal skin, allowing the abdominal wall to stretch and then suturing the peritoneum and the rectus muscles at a second operation five or six days later.

In our series, 9 patients have been successfully operated on. The youngest of these was forty hours old.

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References

1. Hedblom, C. A.: Diaphragmatic hernia: a study of three hundred and seventy-eight cases in which operation was performed. *J. A. M. A.* **85**:947-953, 1925.
2. Orr, T. G., and Neff, F. C.: Diaphragmatic hernia in infants under one year of age treated by operation. *J. Thoracic Surg.* **5**:434-440, 1936.
3. Donovan, E. J.: Congenital diaphragmatic hernia. *Ann. Surg.* **108**:374-388, 1938.
4. Ladd, W. E.: Congenital absence of the pericardium: with report of a case. *New Eng. J. Med.* **214**:183-187, 1936.

INDICATIONS FOR GASTROSCOPY*

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GASTROSCOPY with the flexible gastroscope has now become a generally accepted method of examining the stomach. It gives information regarding the gastric mucosa that is not obtainable by any other procedure. It is particularly important in studying color and detail. Since no other examination gives such information, it is obvious that gastroscopy supplements but does not replace other methods of examination. It is an additional diagnostic procedure of very great value and should be, as Schindler[1] has pointed out, "a routine method of the gastroenterologist, just as cystoscopy is a routine method of the urologist."

The technic of gastroscopy has been fully described,[1, 2] but it may not be amiss to review its essential points, especially those dealing with its simplification. After sufficient experience has been attained, the procedure may be carried out in the office or the outpatient department with the aid of one assistant. X-ray examination of the esophagus and stomach is always carried out before gastroscopy to exclude any esophageal lesion that might contraindicate the blind passage of the gastroscope. This should be done several days in advance so that no barium will remain clinging to the gastric mucosa. The patient should report with an empty stomach; ½ gr. of codeine and 1/150 gr. of atropine are given subcutaneously, and he is instructed to relax for one half to three quarters of an hour. Anesthesia of the throat is then obtained by a 2 per cent Pontocaine gargle. The gargling is done twice; it easily produces satisfactory local anesthesia and eliminates the necessity of any elaborate anesthetizing methods. If there is a history of vomiting or x-ray evidence of pyloric obstruction, the stomach is then emptied of secretions, either by aspirating through a small duodenal tube or by gravity drainage through a

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large stomach tube with the patient in the Trendelenburg position. For this procedure Schindler's special table is very convenient and satisfactory. The best position for gastroscopy is with the patient lying on the left side with the left elbow under the chest, the right arm hanging loosely over the edge of the table and the head extended on small, firm pillows. It has been my experience that patients relax more completely with the head securely supported on pillows than in the hands of an untrained assistant. Since a trained assistant is frequently unavailable, this simplification of the technic has permitted greater independence in the scheduling of cases, and has also given the examiner greater confidence in the handling of difficult patients.

The actual introduction and passage of the gastroscope present no particular problem if proper attention has been given to the preliminary details, especially the correct position on the examining table. With the right hand holding the rigid part of the instrument and the left hand supporting the tip as it enters the patient's mouth, the tongue is depressed by the first two fingers of the left hand, the tip advanced in the midline to the posterior pharynx, the esophageal orifice found and the instrument introduced into the stomach. Much has been written about the advisability of rapid introduction of the gastroscope to avoid spasm, but in my opinion too rapid passage may be dangerous.

The first indication for gastroscopy is gastritis, or suspected gastritis, for it is in the observation of the finer changes in the gastric mucosa that the procedure has its greatest field of usefulness. Since gastritis is the commonest disease of the stomach, the value of gastroscopy is self-evident.

Case Reports

Case 1. J. E. G. (M. G. H. U28421), a 51-year-old white, married American patternmaker, first came to the Out Patient Department in 1925 with a story of gas, indigestion and pain not related to meals. Gastrointestinal x-ray examination at that time showed no definite evidence of organic disease of the esophagus, stomach or duodenum. An additional history obtained at this time showed that the patient took whiskey once a week and chewed tobacco almost continually. Worry was a factor in increasing the symptoms.

Gastroscopy performed on June 7, 1934, showed the pylorus to be normal. Normal rugae were almost entirely absent and were replaced by elevations and depressions of an irregular character. The mucosa was deeper red than usual. The findings were those of hypertrophic gastritis. The patient was placed on a rigid routine, with a six-meal bland diet and complete elimination of alcohol and tobacco. On this regimen he showed moderate improvement. X-ray examination in October, 1936, was again negative. On November 5 gastroscopy was again performed. The rugae were small and presented a beaded appearance throughout the body and fundus of the stomach. The mucosa also was generally verrucous and showed a blotchy reddening. The findings were those of a definite hypertrophic gastritis. At this time it was found that the patient had no free hydrochloric acid in the fasting contents. Dilute hydrochloric acid was given as medication, and the patient was advised to eat liver three times a week. Two months later he was again seen in the Gastrointestinal Clinic; he had gained weight and was feeling better than he had been for 5 years. When last seen in the clinic in September, 1937, he had continued to gain weight and was symptom-free on the regimen described above.

Comment. Gastroscopic examination of this patient, who presented a vague history and negative x-ray examination, permitted a positive diagnosis of hypertrophic gastritis and enabled us to treat intelligently this patient's condition, with notable success. We are accumulating some evidence in this clinic that liver is of benefit in the treatment of gastritis, the rationale of such treatment being the improvement in the atrophic gastritis of pernicious anemia following liver therapy as previously reported by Jones, Benedict and Hampton.[3]

A second very important indication for gastroscopy is unexplained gastrointestinal hemorrhage. A gastroscopic study of patients with hemorrhage from gastritis has recently been reported by Benedict.[4] The following case is a good example.

Case 2. J. G. L. (B. M. U78062), a 69-year-old married American housewife, first entered the Baker Memorial Hospital in September, 1937, complaining of attacks of epigastric pain with nausea and vomiting. These attacks had come on at irregular intervals for a period of fifteen years. The patient had been repeatedly examined at various hospitals, with negative results. For several weeks prior to admission she had passed very dark stools.

The red-cell count on admission was 3,000,000. X-ray examination showed the esophagus to be normal. There was a diverticulum of the posterior wall of the fundus of the stomach near the esophageal orifice. The stomach, pyloric valve and duodenum were otherwise normal except for a second diverticulum off the beginning of the second portion of the duodenum. No cause, however, was found for the gastrointestinal bleeding. A barium enema was negative. A Graham test was also negative. X-ray examination of the upper gastrointestinal tract was repeated on October 14 and again failed to demonstrate any cause for hemorrhage. Gastroscopy performed on October 27 showed the pylorus to be normal, the antrum normal and peristalsis normal. Just proximal to the musculus sphincter antri on the lesser curvature was an erosion 1 mm. deep and 3 mm. in diameter with slightly reddened margins. On the greater curvature there was a definite red streaking of the crest of one fold. There was an area of superficial reddening on the posterior wall in the body of the stomach. The mucosa of the posterior wall in the upper part of the body was markedly verrucous and showed a blotchy reddening. Increase of mucus near the cardiac orifice prevented a satisfactory view of the opening of the diverticulum. Toward the posterior wall, however, a glimpse was obtained of a dark, circular orifice that was probably the narrow mouth of the diverticulum. There was no marked reddening around it. The findings were those of superficial and hypertrophic gastritis with erosions. Continuation of a six-meal bland diet with liver and iron was advised. This recommendation was followed, and the patient has remained well for 2 years.

Comment. This case is typical of many cases of gastric hemorrhage, in which all other methods of examination have been entirely negative, but gastroscopy has revealed

the correct diagnosis and enabled the institution of rational therapy.

It should be emphasized that gastroscopy should be performed within a few days of the hemorrhage, for the delay of even a week will not infrequently mean healing of the gastric mucosa and a false negative examination. No untoward results have been observed from early examination after hemorrhage. It is amazing how rapidly erosions and superficial ulcerations heal and leave no scar whatever. Even true peptic ulcers may heal very rapidly under ideal conditions. In the same way erosions and ulcerations may develop with great rapidity, with resultant almost daily change in the gastroscopic picture. The dictum is, therefore: "Perform gastroscopy early."

A third important indication for gastroscopy concerns cases of so-called "gastric neurosis." That a patient may appear neurotic and x-ray examination may fail to reveal any basis for gastric symptoms does not necessarily mean that no basis exists. Chronic gastritis may be the cause of the symptomatology in such a case and may, in fact, be a contributing factor in the nervous condition of the patient, if a diagnosis of neurosis is justifiable. Chronic gastritis may explain the whole picture, or there may be an additional neurotic element. The following is a case in point:

Case 3. M. E. McN. (M. G. H. U5425), a 39-year-old, married Canadian housewife, first entered the hospital in February, 1933, complaining of almost constant epigastric gnawing and distress, coming on 1 or 2 hours after meals for the last 4 years. There had been some improvement on a six-meal bland diet. A gastrointestinal x-ray examination was negative. The patient was a very nervous woman, with multiple complaints and many worries. A complicating factor was a positive diagnosis of tabes, which made a diagnosis of gastric crises very possible. Since it was necessary to perform a hysterectomy and bilateral salpingo-oöphorectomy for pelvic inflammation in 1932, the condition was also somewhat complicated by menopausal symptoms. Gastrointestinal symptoms, however, persisted, with gurgling and distress in the epigastrium in 1934, bloating and anorexia in 1935 and gas, nausea and gnawing epigastric pain in 1936. In October, 1936, gastrointestinal x-ray examination was again negative.

Gastroscopy on October 23, 1936, showed the pylorus to be normal, the antrum normal and peristalsis normal. The rugae were not enlarged or tortuous. In the upper part of the stomach on the greater curvature and posterior wall there was very marked reddening with a somewhat blotchy appearance. There were also some verrucous elevations in the mucosa of this region. The findings were those of hypertrophic gastritis in the upper part of the stomach. The patient was again put on a six-meal bland diet and advised to take liver four times a week. There was some improvement. In October, 1938, she was again seen in the Gastrointestinal Clinic. She had been adhering more closely to the diet for the last 2 years and had been feeling quite well. Her appetite had improved. At that time she was taking cod-liver oil, yeast and iron. During the last 2 weeks she had had occasional attacks of nausea and vomiting, with pain in the left upper quadrant and along the left costal margin. Further x-ray study and gastroscopy were advised, but have not as yet been carried out.

Comment. This patient's symptomatology might well have been considered due to tabes, artificial menopause and neurosis, but gastroscopy demonstrated a lesion in the stomach as a basis for her symptoms, and treatment of that condition resulted in some improvement. That there has not been complete relief is not surprising when the complicating factors in this case are considered, and when we realize that hypertrophic gastritis is a chronic disease that is frequently difficult to treat.

A fourth use for gastroscopy is in cases where x-ray examination is negative but gastrointestinal symptoms persist. Such a case is the following:

Case 4. M. I. B. (M. G. H. U83951), a 41-year-old, white, married American housewife, entered the hospital in March, 1934, with a 12-year history of gas, epigastric pain, vomiting and tarry stools. X-ray examination had been performed in February, 1933, and had shown a pressure defect on the lesser curvature side of the duodenal cap, probably from the gall bladder. A Graham test done at this time showed no normal filling of the gall bladder, but this was repeated in 1934, when the gall bladder filled normally and the test was considered negative. X-ray examination of the gastrointestinal tract on this admission showed no evidence of organic disease of the esophagus, stomach or duodenum.

Because of the persistence of symptoms, however, gastroscopy was performed on March 22, 1934, and showed 2 erosions of the anterior wall, where the mucosa was granular and nodular. One of the folds of the greater curvature showed a definite clubbing at its crest and an erosion about 2 to 3 mm. in diameter. On the posterior wall in the fundus of the stomach the mucosa appeared pale, with many marked irregular elevations and depressions. The appearance was that of hypertrophic gastritis with erosions. The patient was discharged on a bland diet with belladonna, and was definitely improved 2 months later. Three years later, however, after having reverted to eating only 3 times a day and to smoking cigarettes, she had a recurrence of gas, nausea, occasional vomiting and distress. Further x-ray and gastroscopic examinations were advised but were not carried out.

Comment. This patient's gastrointestinal symptoms were not explained until gastroscopy demonstrated hypertrophic gastritis with erosions. Rational treatment in this case resulted in improvement, but the patient failed to co-operate for a sufficiently long period of time.

Another important indication for gastroscopy concerns cases in which x-ray examination is inconclusive.

Case 5. F. S. T. (B. M. U127931), a 57-year-old, single department manager, was referred for gastroscopy in June, 1938. The patient gave a 2-year history of indigestion and anorexia. X-ray examination on May 12, 1938, showed the esophagus to be normal. The stomach was unusually large and contained a large amount of retained secretion and food. The prepyloric region was not well visualized. The barium passed only in small amounts to this region. The nature of the obstruction in the region of the pylorus could not be definitely demonstrated, but seemed suggestive of ulcer. Re-examination was requested. X-ray examination on May 14 showed a large amount of retained secretion. The barium was very dilute. There was still a large amount of food, but the gastric folds were seen to be considerably thickened, particularly along the lesser curvature and the incisura angularis. No barium passed into the duodenum. Re-examination was

suggested after gastric lavage to determine the cause of the obstruction in the region of the pylorus.

Two days later gastroscopy was performed. In spite of gastric lavage on the ward, preliminary drainage of the stomach with the large stomach tube and the patient in the Trendelenburg position yielded 75 cc. of cloudy, bile-stained secretion. The stomach was again lavaged on the operating table. This secretion contained no free hydrochloric acid. On the lesser curvature near the pylorus was an ulceration about 5 by 3 cm. in size with ragged, nodular, proliferating margins and a dirty-gray base. The ulceration was shallow. The complete pyloric sphincter could not be seen beyond the ulceration, although part of it was visible and gave the impression of being 1 to 2 cm. beyond the ulcer. Higher up in the body of the stomach toward the posterior wall and the lesser curvature there were several smaller nodules of a reddish color, which probably represented a continuation of the malignant process, but might have been due to hypertrophic gastritis. The findings indicated a fairly extensive carcinoma of the stomach, involving the lesser curvature. Because of the extent of the disease and the lack of obstructive symptoms a laparotomy was not advised. Peritoneoscopy[5, 6] was performed on May 23 and showed the liver to be studded throughout with yellowish nodules, varying in size from 3 to 4 mm. to 2 to 3 cm. in diameter, and having the characteristic appearance of carcinoma. A biopsy specimen of the liver at the time of peritoneoscopy showed metastatic carcinoma. X-ray examination on June 16 confirmed the diagnosis of carcinoma, showing a large, dishlike ulceration in the middle of the lesser curvature. X-ray treatment was given, with moderate improvement, but when last heard from the patient was failing rapidly.

Comment. In this case x-ray examination was incomplete on 2 occasions owing to the large amount of retained food and secretion in the stomach. X-ray examination after gastric lavage, as suggested, was not done. Gastroscopic examination resulted in a positive diagnosis of extensive carcinoma. That this was inoperable was demonstrated by peritoneoscopy, at which time a peritoneoscopic biopsy specimen from the liver showed metastatic carcinoma.

Gastroscopy is of value in many cases of gastric ulcer in determining the appearance and location of the lesion and following the healing process. The following is a case in point:

Case 6. S. M. D. (M. G. H. U1997), a 34-year-old housewife, came to the hospital in February, 1938, with a history of epigastric pain, nausea, vomiting and hematemesis. The history was of 14 years' duration, dating back to 1924, at which time x-ray examination showed a duodenal ulcer, and symptoms were relieved by a bland diet. There had been recurring attacks at intervals up to the present entry. X-ray examination in 1936 showed hypertrophy of the gastric rugae, a large ulcer of the lesser curvature of the stomach and a duodenal ulcer. Gastroscopy was suggested by the X-ray Department at this time but was not performed. Gastrointestinal x-ray examination at the present admission showed active gastric ulcer, marked hypertrophic gastritis and an inactive duodenal ulcer.

Gastroscopy was performed on May 26, 1938, and was reported as follows:

> The pylorus is well seen and appears normal. Peristalsis and the antrum are normal. Just at the musculus sphincter antri on the lesser curvature there are 2 ulcers, each about 1.0 to 1.5 cm. in diameter. Both are very shallow and show a clean-gray base with pale margins. They appear to be healing and inactive. The mucosa surrounding the 2 ulcers is essentially normal. There is no evidence of hypertrophic gastritis, although there is some increased reddening, indicating a slight degree of superficial gastritis.

On a rigid medical regimen the patient made an excellent recovery with gain in weight, and was doing very well when last seen 6 months after gastroscopy.

Comment. This case brings up a number of interesting features. In the first place, gastroscopy gave the added information that there was more than one gastric ulcer. This of course is of very great importance with regard to the treatment and prognosis, for a patient with multiple ulcers in the stomach as well as in the duodenum must have a marked tendency toward ulcer formation, and should consequently be particularly careful as to treatment. In the second place, the gastroscopic description of a shallow ulcer with a clean base indicated that both lesions were benign and were healing satisfactorily. In the third place, gastroscopy gave information with regard to the gastric mucosa, which indicated that the gastritis was very slight and superficial, whereas it was described two months previously, following x-ray study, as a very severe hypertrophic gastritis. There can be no question that gastritis may improve very markedly in two months, but that a severe hypertrophic gastritis may revert in that period of time to a slight superficial condition seems rather unlikely, and makes one question the accuracy of the roentgenological diagnosis. Roentgenologists are the first to admit the superiority of gastroscopy over roentgenology in the diagnosis of gastritis.[7, 8] Everyone admits that a negative x-ray examination does not exclude gastritis. Some significance, however, should usually be attached to a positive x-ray diagnosis of gastritis, although it is universally agreed that the roentgenologist cannot classify the types of gastritis or satisfactorily study the progress of the disease.

In cases of duodenal ulcer, gastroscopy not infrequently gives important information regarding the gastric mucosa. It is, of course, impossible to see beyond the pylorus by gastroscopy, and consequently the ulcers of the duodenum cannot be studied. There is often, however, a chronic gastritis associated with duodenal ulcer. After the ulcer is apparently healed the gastritis may persist and cause symptoms. If surgical treatment is contemplated in a case of ulcer of the duodenum, it is important for the surgeon to know the condition of the gastric mucosa. If this is normal, a simple gastroenterostomy or pyloroplasty may be indicated, but if a severe gastritis is present it may be necessary to do a subtotal gastric resection, removing not only the duodenal ulcer but also the diseased gastric mucosa. The following case illustrates this point.

Case 7. L. A. (M. G. H. U18812), a 29-year-old, single American electrician, was first admitted on September 6, 1932, with a complaint of intermittent epigastric pain. The x-ray picture was not characteristic but could have been due to duodenal ulcer. On medical treatment the patient did very well for 4 years.

The second admission was on May 28, 1937, the patient having had recurrence of symptoms with loss of weight. X-ray examination showed an active duodenal ulcer with

moderate pyloric obstruction. Careful medical treatment was again given.

At the third admission, November 13, 1937, there was recurrence of epigastric pain with localized tenderness, and nausea but no vomiting. X-ray examination again showed active duodenal ulcer. Because of the poor response to medical treatment gastroscopy was advised and showed marked hypertrophic gastritis. Because of high acidity and extensive gastritis, partial gastrectomy with removal of the ulcer was advised.

At the fourth admission, December 29, 1937, all consultants agreed that radical operation was indicated. This was performed on January 5, 1938. Gastric resection with posterior Polya anastomosis was performed. The lower half of the stomach was resected. The pathological report showed healing duodenal ulcer with chronic gastritis.

The fifth admission was on November 19, 1938, the patient having remained symptom-free for 11 months following gastric resection. He was then suddenly seized with generalized crampy abdominal pain, causing him to double up. The pain quickly localized in the right lower quadrant. He vomited 3 times and had a chill. At operation a volvulus of the small intestine was reduced with lysis of adhesions. The patient was discharged relieved on December 8.

Comment. This is the history of a patient suffering from duodenal ulcer and chronic gastritis. Surgery was delayed for many years in the hope of obtaining cure on a medical regimen, but no relief was obtained. Gastroscopy showed the extent and severity of the gastritis, which had not hitherto been suspected, and at once gave the indication for radical surgery. The pathological report confirmed the x-ray diagnosis of duodenal ulcer and the gastroscopic diagnosis of chronic gastritis, showing, however, only a small healing duodenal ulcer. The persistent symptoms were quite likely due in large part to the very marked degree of hypertrophic gastritis associated with the duodenal ulcer. So far as his stomach is concerned, this patient has been symptom-free for a period of 1 year since gastric resection.

Similarly in a recent case of duodenal ulcer it was observed that while the ulcer was healing, as shown by x-ray examination, the patient's symptoms were getting progressively worse. Gastroscopy showed a marked degree of chronic hypertrophic gastritis with three superficial ulcerations in the gastric mucosa. It may, therefore, reasonably be concluded that the gastritis and the gastric ulcerations were the cause of his persistent symptoms. From this and other similar observations it follows that no gastrointestinal study is complete without gastroscopic examination.

The importance of gastroscopy in differentiating benign and cancerous lesions has been previously emphasized.[1, 9] Schindler believes that the presence of the circulating blood makes it easier to differentiate cancer and ulcer in the living tissue than in the pathological specimen, even immediately after resection. Most clinicians and pathologists will probably not agree with this, and only gastroscopic observations in a large series of cases will prove or disprove the point. There is no doubt, however, that in certain cases gastroscopy can give valuable information in the differentiation of benign and malignant lesions of the stomach. Technical difficulties such as high position of the stomach or obesity may interfere with satisfactory x-ray examination. Slight rigidity of the gastric wall may give the roentgenologist cause for grave concern, and when there is any doubt, gastroscopy should be performed. The following case exemplifies the assistance given by gastroscopy.

Case 8. W. S. B. (B. M. U129596), a 59-year-old, married American engineer, first entered the hospital on May 24, 1938, with the complaint of intermittent attacks of epigastric pain and indigestion of 30 years' duration. The attacks lasted for 2 to 6 weeks at a time, with severe gnawing epigastric pain associated with gaseous eructations and flatulence. Repeated gastrointestinal x-ray examinations had been negative. A cholecystectomy had been performed at another hospital 29 years previously, without relief.

X-ray examination showed a flat, plateau-like carcinoma of the lesser curvature of the stomach, which was producing obstruction. Gastroscopy showed an ulceration about 2 cm. in diameter, with sharp, red margins and a clean white base, about 2 or 3 cm. proximal to the pylorus. The lesion looked very shallow. The surrounding tissue did not appear indurated. Peristaltic waves seemed to pass over this region. The depth of the ulcer crater did not appear to be more than 2 mm. There was moderate reddening of the mucosa in this region but no evidence of hypertrophic gastritis or of a nodular proliferating lesion. There was a small, red erosion on the crest of a fold of the greater curvature in the body of the stomach. The findings were consistent with a benign ulcer of the lesser curvature near the pylorus. After gastroscopy the x-ray films were checked and found to coincide with the gastroscopic findings. There had been an error in x-ray interpretation.

After 3 weeks of hospitalization on a strict ulcer diet the patient improved markedly. Gastroscopy was then repeated. It showed the lesion to be very much smaller and to have the characteristic appearance of a benign healing gastric ulcer. X-ray examination was also repeated and showed a healing prepyloric ulcer that was still producing incomplete obstruction.

The patient was discharged on the same day very much improved. He has been entirely symptom-free for the last year and a half, feeling better than for many years and working under high pressure.

Comment. The above case illustrates the additional information obtained by a direct view of the lesion through the gastroscope. Until the time of gastroscopy there was a strong possibility of cancer of the stomach, with the certainty of surgical intervention unless that diagnosis was modified. Gastroscopy, however, showed the lesion to be benign, and this has been borne out by the subsequent course of the patient, with complete relief on a strict ulcer regimen.

In certain cases of malignant disease of the stomach gastroscopy is helpful in determining the extent and operability of the lesion.

Case 9. F. D. F. (M. G. H. 333523), a 57-year-old, single American farmer, entered the hospital on November 22, 1933, complaining of indigestion of 6 months' duration gradually getting worse and associated with recurrent vomiting for the last 3 weeks. Physical examination

showed a sense of resistance in the epigastrium, but no definite mass was palpable.

X-ray examination three months before admission was reported as follows:

> The stomach is atonic, and medium in position. Ten per cent residue is present, together with a considerable amount of fluid. The antrum is definitely narrowed. The pyloric valve is constantly spastic. There is a prominent persistent incisura on the greater curvature 5 cm. from the pyloric valve. The lesser curvature is quite straight. Sluggish peristalsis is seen to be present over the stomach. The duodenal cap is never well filled, owing to spasm of the pylorus. The appearance suggests a lesion on the lesser curvature, which is not demonstrated at this examination. Recommend examination of the patient without a motor meal.

A week later the report read:

> Re-examination shows the same process described previously. This has the appearance of carcinoma of the greater curvature of the stomach about 2.5 cm. from the pylorus.

Operation was advised at that time, but the patient refused.

X-ray examination repeated on admission was reported as follows:

> Re-examination with stomach tube confirms the previous findings. There is fixation of the lower 8 cm. of the stomach with deformity of the greater curvature. There is definite evidence of obstruction. The lesion has shown very little gross change in 3 months.

Three days later gastroscopic examination was done and showed a very extensive lesion of the stomach. The report was as follows:

> There is considerable barium in the middle portion of the greater curvature, apparently caught in the folds of the lesion. The lesion itself appears very extensive, probably involving most of the greater curvature and some of both the anterior and posterior walls. The lesser curvature is not well seen. No normal rugae are seen. The appearance is that of extensive ulcerating carcinoma.

From this report it was evident that the disease was very advanced. Exploratory operation was undertaken, however, on November 28, and showed an extensive carcinomatosis, primary in the stomach, with metastatic disease scattered throughout the peritoneal cavity. No resection or palliative procedure was undertaken. Biopsy from one of the metastatic lesions showed carcinoma.

Comment. Gastroscopy in this case showed a much more extensive carcinoma of the stomach than had previously been suspected.

In polyposis of the stomach, gastroscopy frequently gives essential information regarding the size of the lesion, its basal attachment and the general appearance of the surface. Large lesions are almost surely malignant. Lesions with a broad base are likely to be so, and as Benedict and Allen[10] have previously reported, there is likelihood that any adenomatous polyp will become malignant. The gastroscopic appearance of the lesion is therefore of great importance in determining the operative procedure. The following case not only demonstrates the value of gastroscopy in polyp of the stomach but also illustrates another indication for it, namely, observation of the changes in the gastric mucosa in pernicious anemia before and after liver treatment.

Case 10. E. D. S. (M. G. H. U6073), a 67-year-old Canadian street-railway operator, entered the hospital July 3, 1934, complaining of dyspnea and general weakness of 6 months' duration. For the last month nausea and vomiting had been prominent symptoms. Numbness of the fingers and toes had also been noted.

Physical examination showed a fairly well-developed man with a slight icteric tint to the skin. There was slight tenderness in the mid-epigastrium but no palpable mass. The red blood count was 1,400,000, and the hemoglobin 45 per cent. The smear showed marked anisocytosis, moderate poikilocytosis, large macrocytes, microcytes, and reduced platelets.

X-ray examination on June 26, 1934, just prior to admission, was reported as follows:

> Examination of the esophagus is negative. There is an irregular filling defect, showing evidence of craters involving the lower half of the stomach. The duodenum shows a constant deformity that appears extrinsic. The findings are those of carcinoma involving the lower half of the stomach, with an extrinsic compression defect on the duodenum.

On July 5 re-examination by x-ray confirmed the previous observation. The same large defect in the pyloric end of the stomach was noted.

Gastroscopy performed on the following day was reported as follows:

> The entire mucosa is very pale and thin, so that numerous small blood vessels can be seen very well. Normal rugae are almost entirely absent. On the lesser curvature and posterior wall in the antrum of the stomach there is a rounded elevated red lesion, which is fairly smooth in contour and which is attached to the mucous membrane by a broad base. This lesion is about 7 or 8 cm. in diameter and may well be a large benign polyp, but of course there is a very good chance of its now being malignant. The mucosa is typical of the atrophy seen in pernicious anemia. The association of pernicious anemia and polyp of the stomach is so common as to make me believe that the tumor in this case probably arose as an adenomatous polyp.

After liver therapy and transfusion, operation was undertaken on August 7. The following is the operative note:

> A 15-cm. epigastric incision was made. The stomach was delivered without difficulty. In it could be felt a definite polyp. The stomach was opened and arising from the posterior wall, about one third of the way from the pylorus, was a long, tongue-like polyp about 15 cm. in length and ulcerated in two places. It was excised with a wide margin around the base, not making a hole clear through the posterior wall. Immediate examination of the specimen showed no evidence of malignancy. The stomach was closed in three layers with fine catgut.

The pathological report was: "Gastric polyp; no evidence of malignancy."

Following operation the patient made an uneventful convalescence, gained weight and strength, and was able to return to work. Through a misunderstanding he was careless about liver therapy and consequently suffered a relapse 3 months after discharge, but was quickly restored to health after proper treatment was instituted.

Gastroscopy 5 months after operation was reported as follows:

> The mucosa presents a very different appearance from that on previous examination. The color is nowhere very pale though moderately so in some places. In other areas the color is approximately normal, gradually paling off and presenting a somewhat blotchy appearance. Rugae are present along the greater curvature and appear somewhat irregular, but of nearly normal size. There is no evidence of a recurrence of the polyp, but near the antrum some areas show a pseudopolypoid arrangement. I believe there is a chronic gastritis, in a transitional stage perhaps from the atrophic variety seen in untreated pernicious anemia toward the verrucous or hypertrophic type. The findings indicate definite improvement.

Comment. This history records a case of benign gastric polyp associated with pernicious anemia. Gastroscopy revealed a smooth, elongated lesion suggestive of a benign polyp, although malignancy at the base of the lesion could not be excluded. At operation the lesion was demonstrated to be a finger-like benign polyp, which was locally excised with a wide margin. The pathological report showed the lesion to be benign. The association of benign polyp of the stomach with pernicious anemia is too well known to require any comment. The improvement in the gastric mucosa of pernicious anemia seen after liver therapy was first reported by Jones, Benedict and Hampton.[3]

The postoperative examination of the stomach by gastroscopy is of very great value. Many patients after gastroenterostomy or gastric resection continue to have symptoms, some mild and some severe. Some patients complain of the same symptoms that were present before the operation, but many present a vague symptomatology that is often unexplained by the usual studies. Gastroscopy in such cases may demonstrate severe postoperative gastritis.

Case 11. J. E. K. (M. G. H. 30620), a 29-year-old, single American chauffeur, was admitted to the hospital June 9, 1934, because of epigastric discomfort and weakness of 5 days' duration. A posterior gastroenterostomy had been performed 13 years previously at another hospital, when the patient was only 16 years old, because of symptoms thought to be due to a duodenal ulcer. Following operation the patient had a return of his original symptoms, accompanied by hematemesis and melena. No duodenal ulcer was demonstrable by x-ray examination. Because of hemorrhage, exploratory laparotomy was performed, with pylorectomy. No duodenal ulcer was demonstrable. The gastroenterostomy stoma appeared normal.

The second admission was on June 8, 1935, because of tarry stools. X-ray examination showed a well-functioning anastomosis, dilatation of the anastomosed jejunum and marked swelling of the gastric rugae.

The third admission was on November 27, 1935, because of severe hematemesis and melena. The red-cell count was 1,500,000. Gastroscopy at this time showed what appeared to be old blood in the stomach, with reddening and erosions of the mucosa. It was believed that much of the hemorrhage came from severe postoperative gastritis. X-ray examination showed thickened mucosal folds with deep crypts between them, simulating ulcer craters. No definite ulcer could be demonstrated.

The fourth admission was on March 18, 1937, because of severe recurrent hematemesis after considerable alcohol intake. The red-cell count was 1,100,000. X-ray examination showed marked swelling of the rugae about the stoma but no definite ulcer. Gastroscopy was not done.

The fifth admission was on September 14, 1937, because of the recurrence of severe hematemesis, with the red-cell count 1,800,000. X-ray examination again showed hypertrophy of the gastric rugae but no definite ulcer and no evidence of esophageal varices. Gastroscopy showed evidence of a marked hypertrophic gastritis, that is, increased reddening and a verrucous appearance of the mucosa, with one erosion.

The sixth admission was on January 16, 1938, because of melena. The red-cell count was 3,000,000. X-ray examination and gastroscopy were not done.

The seventh admission was on May 19, 1938, because of the passage of a large tarry stool. The red-cell count was 3,000,000. Gastroscopy showed a marked improvement in the gastric mucosa. X-ray examination showed no ulcer and no swelling of the mucosa.

The eighth admission was on January 9, 1940, because of recurrent hematemesis. The red-cell count was 1,900,000. X-ray examination again showed no ulcer, but there was a widening of the gastric rugae. Gastroscopy showed increased reddening of the mucosa, with exudate in the valleys between the folds. There was old blood in the stomach, a cobble-stone appearance on the posterior wall and several areas of erosion and ulceration. The findings indicated superficial and hypertrophic gastritis with erosions. Gastric resection was advised but refused.

The ninth and final admission was on August 27, 1940. During the 8 months since the previous admission the patient had been fairly comfortable until shortly before being admitted, when he passed a tarry stool. The red-cell count was 3,600,000 but rose after transfusion to 5,000,000. At this time the patient agreed to subtotal gastric resection, which was performed. The convalescence was uneventful. Pathological examination showed a very red and injected gastric mucosa with prominent rugae. One cubic millimeter from the posterior gastroenterostomy stoma there was a small punched-out erosion 4 mm. in diameter. The pathological diagnosis was chronic gastritis.

Comment. This case is one of a young man repeatedly admitted to the wards of the hospital for very severe hemorrhage. At no time was it possible to demonstrate anything more than severe gastritis as the cause of hemorrhage. Gastroscopy repeatedly showed the degree of gastritis present — very severe with multiple erosions at some examinations but with nearly normal mucosa at others. Because of the many recurrences of severe hematemesis, subtotal gastrectomy was performed. The pathological report of chronic gastritis with erosion confirmed the gastroscopic and x-ray findings. No ulcer was present. Severe hemorrhage from gastritis is one of the few indications for resection in this disease.

This case demonstrates that severe postoperative gastritis is a very real entity and may be the cause of severe symptoms. The progress of the disease is best followed by repeated gastroscopic examinations.

Another indication for gastroscopy is the presence of a foreign body in the stomach. In known cases the open-tube gastroscope[11] has been used for many years in removing such bodies. The new flexible gastroscope, however, may be useful in differentiating a polyp in the stomach from a

foreign body, as shown by the following unusual case.

CASE 12. E. D. (M. G. H. U29583), a 43-year-old, married, American housewife, first entered the hospital on April 24, 1937, because of epigastric distress of 2 years' duration. A diagnosis of peptic ulcer had been made 20 years previously, at which time she had obtained relief by following a diet. X-ray examination showed multiple extensive defects in the lower two thirds of the stomach; these could not be moved on palpation but had the appearance of food. There was a definite lesion in the pylorus — probably ulcer. The report of a repeated x-ray was as follows:

> There is narrowing of the prepyloric region, with at least three grape-shaped defects in the prepyloric area. At least two of these defects can be moved away from this area and brought into the body of the stomach. The findings are those of a lesion in the prepyloric region. The defects described are present in spite of stomach lavage, and are identical with those seen at the previous examination. Their extreme mobility and the absence of a demonstrable pedicle are against a polyp, which, however, is still considered the most likely diagnosis. Recommend gastroscopy.

Gastroscopy was performed May 1, 1937. The report was as follows:

> Just inside the cardiac orifice on the greater curvature a purplish-black, irregularly shaped object about 1 to 2 cm. in diameter is clearly visible and appears to lie free and movable in the stomach cavity. It is probably a foreign body. Just proximal to it is a second object of a yellow color about 1 cm. in diameter, shaped like a fruit stone, which also appears to be lying free. The mucosa in general is of normal color, but there are numerous small areas in the fundus and antrum, indicating erosions. The pylorus and antrum are well seen. Normal peristalsis is passing over the antrum. No polyp or carcinoma is visible, the only abnormality in the mucosa being the few erosions described. Diagnosis: foreign bodies of the stomach; superficial gastritis, with erosion.

Because of the underlying pyloric ulcer with pyloric obstruction these foreign bodies would not pass the pylorus, in spite of dietary regimen and belladonna. Although it would probably have been possible to remove these bodies through the open-tube gastroscope, it was thought that surgical intervention was indicated to treat the pyloric ulcer and that at the same time the foreign bodies could be removed. Laparotomy was therefore undertaken on May 11. An incision was made in the anterior wall of the stomach, and a prune stone and a plum stone were extracted. A definite ulcer was felt in the prepyloric region. The ulcer was resected, and a Finney pyloroplasty performed. The pathological report read "acute and chronic gastritis."

The convalescence was uneventful. Three and a half years after the operation the patient was seen in the Out Patient Department. She was symptom-free and had gained 20 pounds in weight.

Comment. This case represents an unusual type of gastrointestinal problem in which the final diagnosis was definitely established by gastroscopy.

DISCUSSION

From a study of the material presented above it is evident that gastroscopy has added greatly to knowledge of disease of the stomach. Gastroscopy is a practical method of examination that gives us information regarding the color and detail of the gastric mucosa not obtainable in any other way.

Chronic gastritis is the commonest disease of the stomach; it is difficult to diagnose clinically, but easy by gastroscopy. Therefore patients with vague gastrointestinal complaints and negative x-ray examination should have gastroscopic examination. Hemorrhage from gastritis is now a well-recognized clinical entity. Severe bleeding may come from gastritis alone, and may occasionally call for gastric resection. Gastroscopic examination is necessary to establish a positive diagnosis and to follow the course of the disease. The examination should be made within a few days of the bleeding, since otherwise erosions and superficial ulcerations, which may have been the cause of severe hemorrhage, may have healed completely, leaving the diagnosis still in doubt. In cases of duodenal ulcer with hemorrhage the bleeding may in some cases be coming not from the ulcer but from the associated gastritis. The importance of recognizing this is obvious, for if surgery is to be undertaken a knowledge of the degree and extent of the gastritis is essential in order to plan an adequate operation. If there is very little gastritis a small partial resection may suffice; if there is moderate gastritis confined to the lower part of the stomach the resection should be planned accordingly; if there is very severe, extensive gastritis involving the upper part of the stomach, it may be advisable to continue medical treatment, postponing surgery indefinitely.

A diagnosis of gastric neurosis is not justifiable until gastroscopic examination has ruled out organic disease of the stomach. If chronic gastritis is present it may be the entire cause of the patient's symptoms or at least a major contributing factor. On the other hand, if no lesion is demonstrable either by x-ray or by gastroscopy the patient may rationally be treated for gastric neurosis. Similarly, when gastrointestinal symptoms persist in the presence of negative or inconclusive x-ray examinations, gastroscopy may establish a positive diagnosis. In fact, no gastrointestinal study is complete without gastroscopy.

Various problems arise in the diagnosis and treatment of peptic ulcer, some of which may be solved by direct inspection of the gastric mucosa. Gastroscopy may reveal one or more gastric ulcers not previously suspected. Such an observation will naturally modify the treatment. Direct inspection of an ulcer during treatment will be of assistance in evaluating the progress of the healing process. The demonstration of a severe gastritis in association with either a duodenal or a gastric ulcer will

sometimes modify the treatment and prognosis. A duodenal ulcer, for example, may appear to be healing, yet clinically the patient is getting worse; in some such cases it is the severe associated gastritis that is giving the symptoms. The question of cancer is always of great importance in gastric ulcer. By demonstrating that an ulcer has sharp margins and a clean base the gastroscopist can make a diagnosis of benign ulcer; if the margins are slightly irregular or the base dirty a diagnosis of cancer must be made. There are of course cases in which there will be doubt clinically, roentgenologically and gastroscopically; such cases must be regarded as cancerous until proved otherwise.

In suspected cancer of the stomach gastroscopy may establish a positive diagnosis. In occasional cases, when other methods of examination have failed, gastroscopy has demonstrated advanced carcinoma. Help may be given to the surgeon by the gastroscopic demonstration of the extent and operability of a gastric tumor. In the differential diagnosis of hypertrophic gastritis, carcinoma and lymphoma, gastroscopy, although not always giving the correct diagnosis, has been of definite assistance.

It is frequently said by roentgenologists that the stomach is difficult to examine postoperatively. In cases of postoperative gastritis, jejunal ulcer or recurrent neoplasm, gastroscopy has given valuable assistance. Postoperative gastritis is a distinct entity, which is impossible to evaluate or to treat satisfactorily without gastroscopy. Severe cases with hemorrhage may require further surgery.

In polyposis of the stomach, gastroscopy may differentiate true polyps from enlarged folds or foreign bodies, and in the former will demonstrate the broadness of the base and ulceration of the surface, vital factors in deciding the question as to whether malignant degeneration has occurred.

Lest the reader receive the impression that gastroscopic examination is the final answer to all problems in gastric diagnosis, it should be pointed out that there are definite limitations to gastroscopy. There are a few patients who cannot be satisfactorily examined because of inability to extend the head, obstruction of the esophagus, spasm of the stomach, lack of co-operation and so forth. In ninety-nine cases out of a hundred, however, it is possible to effect a satisfactory introduction of the gastroscope. The examiner is then faced with the problem of visualizing all parts of the stomach. Because of the irregular shape of the organ certain areas are difficult to inspect, namely, the lesser curvature near the pylorus, the greater curvature near the angulus and the posterior wall near the cardia. However, by proper manipulation of the instrument and the patient, and by observation during various phases of respiration and peristalsis, many of these so-called "blind areas" can be eliminated. A third difficulty is the correct interpretation of the findings. For example, the experienced observer knows that minor changes in the gastric mucosa may not be the cause of symptoms, that severe hypertrophic gastritis may be confused with an infiltrating type of carcinoma and that a benign gastric ulcer cannot always be differentiated from an early malignant gastric ulcer. Gastroscopy thus has its limitations. With increasing experience, however, and with improvements in the instrument, such as the biopsy forceps recently described by Kennamore,[12] gastroscopic examination is bound to play an increasingly important role in the diagnosis and treatment of gastric disease.

Conclusions

Gastroscopy is now a generally accepted method of examining the stomach. It bears much the same relation to gastroenterology that diagnostic cystoscopy bears to urology.

Gastroscopic examination is easily conducted in the outpatient department with the aid of only one assistant. The technic of local anesthesia is simplified by merely having the patient gargle with a 2 per cent solution of Pontocaine. A specially trained head-holder is unnecessary, since the procedure is very satisfactorily carried out with the head resting on small pillows.

The various indications for gastroscopy are given and 12 illustrative cases are presented and discussed.

References

1. Schindler, R.: *Gastroscopy: the endoscopic study of gastric pathology.* 343 pp. Chicago: University of Chicago Press, 1937.
2. Benedict, E. B.: Examination of the stomach by means of a flexible gastroscope: a preliminary report. *New Eng. J. Med.* **210**:669-674, 1934.
3. Jones, C. M.; Benedict, E. B., and Hampton, A. O.: Variations in the gastric mucosa in pernicious anemia: gastroscopic, surgical and roentgenologic observations. *Am. J. M. Sc.* **190**:596-610, 1935.
4. Benedict, E. B.: Hemorrhage from gastritis: a gastroscopic study. *Am. J. Digest. Dis. & Nutrition* **4**:657-664, 1937.
5. Ruddock, J. C.: Peritoneoscopy. *Surg., Gynec. & Obst.* **65**:623-639, 1937.
6. Benedict, E. B.: Peritoneoscopy. *New Eng. J. Med.* **218**:713-719, 1938.
7. Schatzki, R.: The comparative value of gastroscopy and roentgen examination of the stomach. *Radiology* **29**:488-491, 1937.
8. Ansprenger, A., and Kirklin, B. R.: Roentgenologic aspects of chronic gastritis: critical analysis. *Am. J. Roentgenol.* **38**:533-541, 1937.
9. Benedict, E. B.: Gastroscopic observations in neoplasm. *New Eng. J. Med.* **214**:563-566, 1936.
10. Benedict, E. B., and Allen, A. W.: Adenomatous polypi of the stomach: with special reference to malignant degeneration. *Surg., Gynec. & Obst.* **58**:79-84, 1934.
11. Jackson, C., and Jackson, C. L.: *Bronchoscopy, Esophagoscopy and Gastroscopy: A manual of peroral endoscopy and laryngeal surgery.* Third edition. 485 pp. Philadelphia: W. B. Saunders Co., 1934.
12. Kennamore, B.: personal communication.

PULMONARY INFARCTION AS A CAUSE OF PNEUMOTHORAX

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SPONTANEOUS pneumothorax is an infrequent complication of pulmonary disease as seen in a general hospital. There is frequently, and quite properly, a tendency to attribute the condition to tuberculosis, but if there is little or no evidence of a pre-existing tuberculous infection, other causes should also be considered. The standard textbooks of medicine list a variety of conditions as possible causes of spontaneous pneumothorax and are in general agreement as to their relative importance as etiologic factors. During recent years, attention has been called to the frequency of rupture of an emphysematous bleb as the reason for an otherwise unexplained pneumothorax. It is agreed that an infarct, if septic, may break down and permit the passage of free air into the pleural cavity. It is fortunate that the latter does not often happen, since pulmonary infarction is a not uncommon complication in postoperative patients and in others whose circulation is inadequate.

Infarcts of the lung are usually of recent origin when first seen, and they will usually be found to have changed appreciably in size or radiographic density if repeated examinations are made during the ensuing few days. This relatively rapid change in the lesion as shown on serial roentgenograms calls attention to the fact that the process is an acute one and therefore unlike the usual tuberculous process, which, though active, is not likely to change definitely in appearance within the space of a few days. If necrosis occurs within the infarcted area and pneumothorax results, there is likely to be a rapid outpouring of purulent exudate, thus giving rise to a pyopneumothorax.

Pulmonary infarction is secondary to a pathologic process elsewhere in the body. If, therefore, a pneumothorax is found in a patient known to have a disease that may give rise to the formation of emboli, infarction should be considered as a possible cause of the pneumothorax. The possibility becomes a probability if an area of consolidation is present at or near the base of the lung, and especially if there is an inflammatory process elsewhere in the body. The following two cases are illustrative of these facts.

CASE REPORTS

CASE 1 (N. E. D. H. 86423). The patient was a 17-year-old boy who was first seen in the New England Deaconess Hospital in March, 1937, at which time he was suffering from a moderately severe ulcerative colitis of recent onset. He was under the care of Dr. E. P. Joslin and his associates. He remained in the hospital 36 days and during the latter part of his stay had only one stool daily. During this time he gained 8 pounds, and the temperature and pulse were essentially normal.

The patient was readmitted to the hospital during August, 1937, and again in June, 1938, because of recurrence of the diarrhea, with the occasional passing of blood.

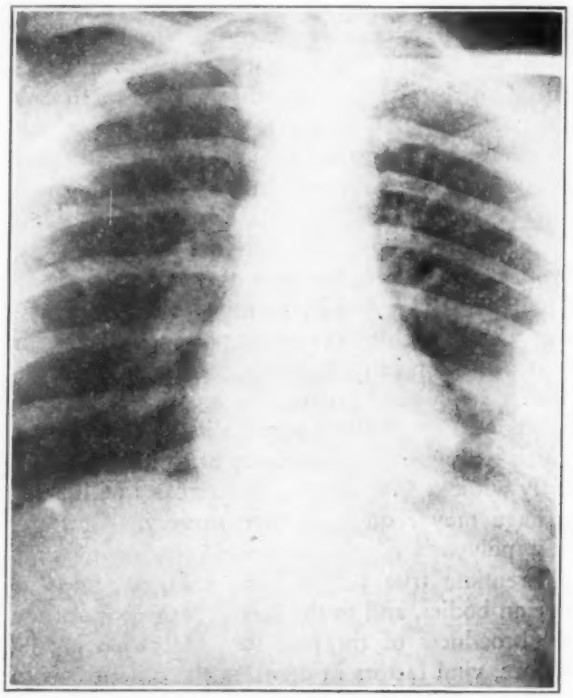

FIGURE 1. *Case 1.*

This film was taken on the third hospital day. There is consolidation at the left base laterally.

Proctoscopy and roentgen examination with barium enema showed findings characteristic of ulcerative colitis. He was discharged on July 12, 1938, and it is interesting that the record shows that physical examination of the chest on that day was entirely negative.

The patient was again admitted to the hospital 10 days later, this time because of nausea, vomiting and hematemesis. There had been no cough or dyspnea. He stated that he had vomited some dark, bloody material, and was sure that this had not been coughed up. Physical examination showed a pale, slightly cyanotic young adult who was perspiring freely. The temperature was 102°F., and the pulse 120. The lungs were clear except for a triangular area in the left axilla, over which there was some dullness, and diminution of breath sounds. X-ray examination of the chest with a bedside unit on the 3rd hospital day showed an area of consolidation at the left base laterally, including the costophrenic angle and extending upward to the level of the 4th rib in the axilla. A second exam-

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ination on the 19th hospital day showed a slight decrease in size and density of the area of consolidation previously noted, but there was then a small amount of free air in the left pleural cavity, and a new area of partial consolidation opposite the right second interspace.

One week later the degree of pneumothorax on the left was somewhat more marked, the degree of collapse of the lung being estimated at 60 per cent. Several areas

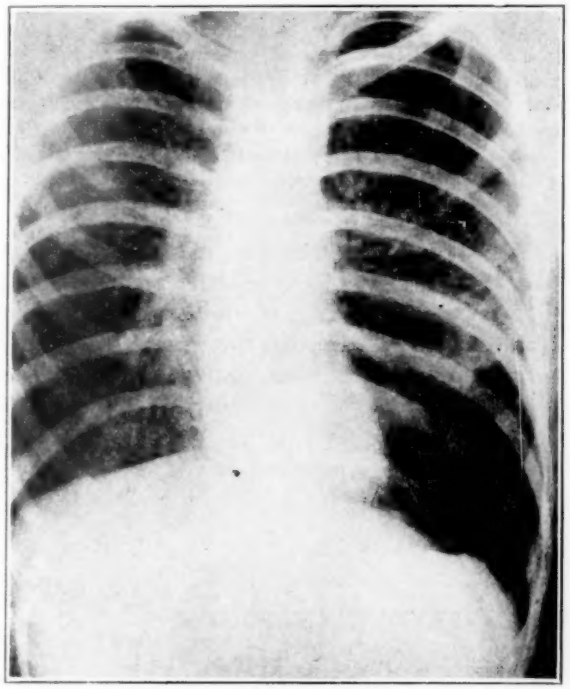

FIGURE 2. *Case 1.*

This film was taken on the twenty-sixth hospital day. There is pneumothorax, with partial clearing of the consolidated area.

of diminished density within the original area of consolidation suggested multilocular cavity formation.

There was some cough and expectoration at this time, and examination of the sputum showed a few suggestive acid-fast organisms. Subsequent examinations failed to show similar organisms, and a guinea pig inoculated with the sputum revealed no evidence of tuberculosis.

On the 22nd hospital day it was noted that the general condition was distinctly worse. There was elevation of the pulse and respiratory rates, and slight cyanosis. On the following day the patient complained of pain in the right thigh, but there was no redness or swelling. The temperature at this time was 103°F., but it subsequently fell gradually, and was practically normal at the time of his death on the 38th hospital day. The pulse rate remained elevated. During this stay in the hospital he had passed two or three loose stools daily that showed positive benzidine tests for blood on almost all examinations, although there had been no gross bleeding.

Autopsy. There was free air in the left pleural cavity, and adhesions extending from the region of the interlobar fissure to the parietal pleura in the axillary line. The right and left lungs weighed 600 and 410 gm., respectively. Several areas of consolidation were present in each lung. These were roughly pyramidal in shape, with their bases at the pleural surface. Adherent thrombi were found in several branches of the pulmonary artery on the right, but none were found on the left. Injection of air into the left main bronchus failed to demonstrate the point of leakage. The descending colon showed several irregular, superficial areas of ulceration, with hyperemia of the surrounding mucosa. In the right internal and external iliac veins there was a closely adherent thrombus that varied from red to gray. All other organs and tissues were essentially normal.

CASE 2 (N. E. D. H. 97823). A 24-year-old, unmarried, man was admitted to the hospital on July 29,1939, on the medical service of the Lahey Clinic, with a complaint of increasing weakness and shortness of breath. He had been well until 1 year previously, when he had developed a hacking, nonproductive cough. He had consulted a local physician and been told that he had "heart trouble." He had given up his work as a counterman and had been fairly well until 3 months before admission, when he had consulted another physician and had been told he had "thyroid trouble." During the 10 weeks prior to admission he had been a patient in a nearby hospital. He had lost a total of 80 pounds during the year.

He had had scarlet fever and probably also tonsillitis, but there was no history of rheumatic fever, pleurisy, pneumonia, influenza, tuberculosis, gonorrhea or syphilis.

Physical examination showed a pale, slightly jaundiced young male adult who was dyspneic and orthopneic. The

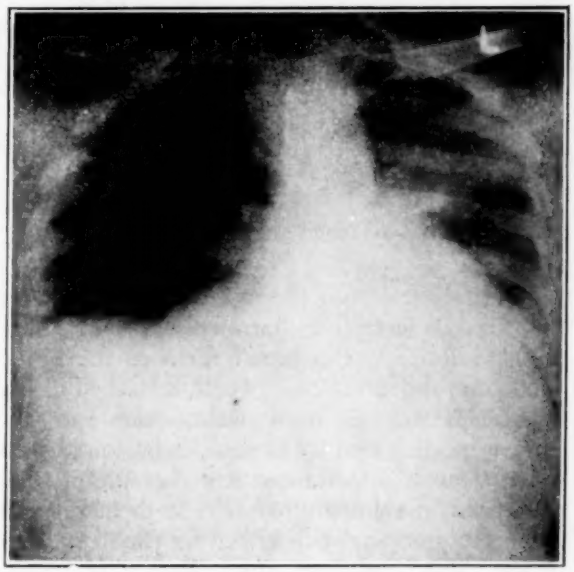

FIGURE 3. *Case 2.*

Hydropneumothorax, with an Area of Consolidation on the Opposite Side.

extremities were cold and slightly edematous. There was dullness at the left base with diminished breath sounds, and there were rales at both bases. The heart was greatly enlarged and showed a gallop rhythm and a systolic murmur at the apex. The liver edge extended about 5 cm. below the costal margin. There was no clubbing of the fingers, and no petechiae were seen. The blood pressure was 110/70. The red-cell count was 3,600,000, and the white-cell count 18,750. The serum protein was 4.9 gm. per 100 cc., and the nonprotein nitrogen 86 mg. per 100 cc. An electrocardiogram taken on the day of admission showed slurring of the QRS complex in all leads, left-axis deviation and slight inversion of T_1.

Respiration was improved following withdrawal of about 2500 cc. of amber-colored fluid from the left pleural cavity. Digitalization and the intravenous administration of Salyrgan produced a moderate diuresis, with decrease in size of the liver and disappearance of the edema of the lower extremities. The nonprotein nitrogen in the blood gradually increased in amount, and the breath became uriniferous.

On the 18th day the patient developed pain in the right lower thorax, accompanied by an increase in the pulse and respiratory rates. X-ray examination of the chest at this time showed a hydropneumothorax on the right, with approximately 80 per cent collapse of that lung, and with a slight shift of the mediastinum toward the left. There was an area of mottled consolidation in the left lung opposite the 2nd interspace anteriorly. The heart appeared moderately enlarged. X-ray examination on the 2nd day had shown high position of both diaphragms, congested lungs, a small amount of fluid in the right pleural cavity and enlargement of the heart, but no evidence of pneumothorax.

There was a rapid increase in dyspnea, and since the findings suggested a positive pressure pneumothorax, a needle was inserted in the right pleural cavity. The initial pressure was equivalent to 9 cm. of water, but after removal of 1700 cc. of air, the pressure was 2 cm. on expiration, with a negative pressure of 5 cm. on inspiration. The withdrawn air had a foul odor suggesting hydrogen sulfide. Death occurred 2 days later.

Autopsy. The right pleural cavity was opened under water. Foul gas escaped under pressure, and there was also 3000 cc. of greenish-brown fluid having a foul odor. The pleura was thickened and was covered by a shaggy exudate. The left pleural cavity was not remarkable. The pericardial cavity contained 400 cc. of clear, brownish fluid, and the pericardium was covered with a shaggy exudate. The heart weighed 620 gm., but its valves and coronary arteries were normal. The cut surface of the myocardium was a deep red, with scattered streaks of brownish yellow near the apex. The right and left lung weighed 440 and 320 gm., respectively. The right upper lobe and both lobes on the left contained several firm foci measuring 2 to 3 cm. in diameter. The right middle and lower lobes were gangrenous. An adherent, gray thrombus was found in one of the branches of the right pulmonary artery. Other findings included an adrenocortical adenoma and a mid-zonal cirrhosis of the liver.

SUMMARY

Two proved cases of pneumothorax resulting from pulmonary infarction are presented. Although pneumothorax is a rare complication of infarction, it is believed that the clinical history and roentgen findings are sufficiently clear in most cases to suggest the correct diagnosis.

I am indebted to Drs. E. P. Joslin and F. H. Lahey for their permission to report these cases.

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THE SIGNIFICANCE OF CHARCOT-LEYDEN CRYSTALS*

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THE crystals now known as Charcot-Leyden crystals were first described in 1853 by Charcot and Robin,[1] who found them in the heart's blood and the spleen of a patient who died of leukemia. It was not until twenty years later that they were described by Leyden,[2] who found them in *"asthmatic"* sputum and who, because of slight variations in solubility, considered them different from those originally described by Charcot. Even before this second description, Böttcher[3] had found in prostatic secretion crystals that for the next three decades were generally accepted as identical with the Charcot crystals. As a result, considerable confusion arose in the literature; in fact, much of the chemical investigation done on the crystals obtained from prostatic secretion was incorrectly applied to the Charcot-Leyden crystals.[4, 5] The latter were first described in this country in a case of leukemia by White[6] in 1859. In 1895, Cohn[7] reviewed the literature and concluded that the crystals found in leukemic blood, in asthmatic sputum, in nasal polyps and in bone marrow differed from those found in prostatic secretion. The relation of Charcot-Leyden crystals to eosinophils was first emphasized by Schwarz[8] in 1914. In 1921, Liebreich's[9] description of the appearance of the crystals in normal blood reawakened interest in the subject. This description was confirmed by Neumann[10] several years later. Wrede,[11] in 1927, revived the older theory of the relation of the prostatic to the leukemic crystals, and by questionable chemical methods showed a higher concentration of "spermin" in leukemic than in nonleukemic spleens. Since then the literature[12, 13] has been chiefly confined to an occasional observation of Charcot-Leyden crystals in various pathologic conditions such as eosinophilia of unknown cause and periarteritis nodosa. Turner et al.[14] in 1936, suggested that the substance in the eosinophil apparently responsible for the so-called "Gordon phenomenon" was the Charcot-Leyden crystal, although the reference they gave contained no mention of such a relation.

The present study deals with attempts to demonstrate Charcot-Leyden crystals in blood and tissues and to determine their nature.

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Methods

In the routine demonstration of Charcot-Leyden crystals a drop of the material to be examined was placed on a glass slide and protected from evaporation by shielding it with a coverslip ringed with vaseline. The slide thus prepared was allowed to stand at room temperature for at least a week and was examined daily under the microscope. The Charcot-Leyden crystal was considered to consist of two symmetrical, six-sided pyramids joined base to base. They were always readily identifiable under the high dry lens of the microscope, varying in length from one half to three times the diameter of an erythrocyte (Figs. 1 and 2). Usually they were first seen on the fourth day.

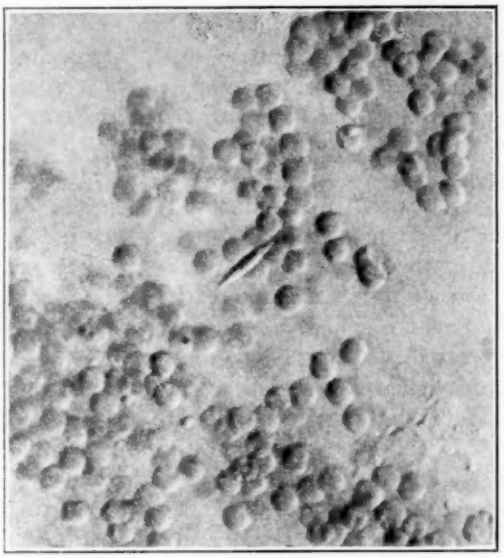

Figure 1. *Photograph of a Charcot-Leyden Crystal in the Blood of a Patient with Periarteritis Nodosa.*

Sources

From 100 routine hospital medical admissions, drops of finger blood were obtained and a wet smear was made. The patients represented a variety of diseases including hypertension, chronic nephritis, heart disease, pernicious and aplastic anemia, peptic ulcer, pneumonia, carcinoma and various types of lymphoma, including myelogenous and lymphatic leukemia, lymphosarcoma and Hodgkin's disease. The white-cell counts ranged from 3000 to 240,000, and the percentages of eosinophils from 0 to 25, the highest figure being associated with a leukopenia. The blood of none of these showed an absolute increase of the eosinophils, and in no blood were Charcot-Leyden crystals demonstrated.

Several patients were studied in particular because of their disease or because of an unusual eosinophilia. Of 5 patients with bronchial asthma with an average eosinophilia of 8 per cent, none showed crystals in the blood. One patient with chronic ulcerative colitis had typical crystals in the stools but not in the blood. Of 3 patients with chronic myelogenous leukemia, 2 showed a number of crystals in the blood. Their respective white-cell counts were 55,000, with 12 per cent eosinophils, and 78,000, with 14 per cent eosinophils. Two cases of presumed periarteritis nodosa showed Charcot-Leyden crystals in large numbers in the blood by the usual wet-smear method; the white-cell counts were 20,000, with 70 per cent eosinophils, and 40,000 with the same percentage of eosinophils. One case of presumed trichiniasis with a white-cell count of 16,000 and a 20 per cent eosinophilia showed an equally large number of crystals.

The blood of horses used for the production of anti-serum,* studied by the usual method, showed little eosinophilia and no crystals.

Figure 2. *Photograph of Four Charcot-Leyden Crystals in a Bronchiolar Mucous Plug in a Patient Dying of Bronchial Asthma (highly magnified).*

The crystal on the left is cut across and shows the hexagonal shape.

Normal rabbits' blood showed no crystals even though their neutrophilic cells have an eosinophilic cast.

Five guinea pigs were inoculated with *Trichinella spiralis*. The maximum eosinophilia thus obtained was 20 per cent, with a white-cell count of 10,000. No crystals were obtained.

Prostatic secretion, obtained post mortem, produced no Charcot-Leyden crystals on standing for a week. After the addition of lead acetate to a

*Obtained through the courtesy of the Antitoxin and Vaccine Laboratory, Massachusetts Department of Public Health.

filtered alcoholic solution of the secretion as described in the literature,[15] quadrilateral crystals were found, which because of the number of plane surfaces, lack of symmetry, and spindling tendency we did not consider characteristic of Charcot-Leyden crystals. They did, however, resemble those crystals depicted in the literature as being typical of "spermin."[16]

The work of Liebreich[9] was repeated in part in an attempt to produce Charcot-Leyden crystals from normal blood. The various methods that he proposed consist essentially of a concentration of the white-cell layer. Contrary to his claim, eosinophils were not thus produced, nor were Charcot-Leyden crystals found after allowing a wet smear of such a preparation to stand. After several days, long spindling crystals, without plane surfaces, appeared and were thought possibly to be fibrin.

Microscopical sections of tissues from 11 fatal cases of myelogenous and lymphatic leukemia were examined. The preparations from only 1 case showed the crystals; they were visible in all tissues of the body and were most plentiful in the pancreas and spleen. This patient had myelogenous leukemia. Only occasional eosinophils were found in the peripheral blood, but eosinophils were markedly increased in the bone marrow and lymph nodes. Of 7 patients with ulcerative colitis in whom sections of the colon were examined post mortem, 1 showed a marked increase of eosinophils in the submucosa, with occasional small Charcot-Leyden crystals.

Slides of the lungs obtained from 8 fatal cases of bronchial asthma were reviewed. In 1 case crystals were found in the mucus plugging the smaller bronchioles.

Nature of the Crystals

The exact nature of Charcot-Leyden crystals has never been determined. Earlier investigations have been clouded by confusion with the crystals obtained from prostatic secretion. In the earlier literature it is said[7, 15] that Charcot-Leyden crystals are soluble in hot water, acetic acid, tartaric acid, phosphoric acid, potash and sodium, but not in cold water, alcohol, ether, chloroform and glycerin.

Using the blood obtained from a case of trichiniasis, where Charcot-Leyden crystals of a typical shape had been found in great numbers, the solubility of the crystals was tested in tap water, distilled water, ethyl alcohol, glycerin, sodium hydroxide, formalin, acetic acid, sulfuric acid and nitric acid, all in various dilutions. In all these solutions the crystals were dissolved or destroyed, disappearing by fragmentation at varying speeds. Neither by drying nor by adding substances of the opposite reaction, nor by further dilution, were the crystals again seen in solutions so treated.

A small hanging-drop preparation of the crystals was incubated with pepsin for forty-eight hours. At the end of this time the crystals had disappeared. In a similar preparation incubated without pepsin but with physiological saline solution the crystals persisted, apparently unchanged.

Because of the work of Code and MacDonald[17] suggesting some parallelism between human eosinophils and a histamine-like substance, both normal and eosinophilic blood samples were combined in various dilutions with histamine and histaminase. Wet-smear preparations of these mixtures produced no Charcot-Leyden crystals.

Discussion

It is apparent from this study that the appearance of Charcot-Leyden crystals, when considered only in their typical form, shows a close relation to eosinophils, since the crystals were found in blood where a high absolute eosinophilia existed, whereas they were not demonstrable by the same technic when eosinophils were not present in abnormally high numbers. This association has been pointed out in the literature and in general has been found to be true wherever the crystals have appeared.[8]

According to our work and according to the literature, the crystals are apparently not specific for any disease. They have been found in the blood from cases of the lymphoma group, periarteritis nodosa, trichiniasis and other diseases associated with an eosinophilia[12, 13]; in the stools of patients with a variety of intestinal infections[18]; in the sputum of asthmatic patients and those with other types of bronchial disease[2, 12]; in pleural fluids[19]; and in such localized collections of eosinophils as nasal polyps and skin blebs.[8] In all these cases the relation of the crystals to the eosinophils seems to hold true.

The nature of the crystals is not known. No recent chemical work has been done on the subject, and the crystals have never been isolated from the materials in which they were found. The chemical determinations done on prostatic secretion do not apply, since the true Charcot-Leyden crystal shows a different architectural pattern and has never been proved to be identical or transmutable chemically. The isolation and analysis of these crystals should help in the understanding of the eosinophil.

Summary

Typical Charcot-Leyden crystals were found in the blood of all patients with a high absolute

eosinophilia, but were not found in the 102 cases where eosinophilia was not present. They were also found in suitable preparations of tissues with a marked local eosinophilia.

Investigation of the blood of guinea pigs, horses and rabbits, after the administration of various stimuli, yielded no crystals; however, the blood eosinophilia never reached a high absolute level.

Attempts to isolate the crystals from the blood were unsuccessful. In a variety of solutions tried they were either dissolved or destroyed.

The crystals do not appear to be typical of any specific disease, but seem rather to be associated with eosinophilia, whether generalized or localized.

REFERENCES

1. Charcot, J. M., and Robin, C.: Observation de leucocythemie. *Mem. de Soc. de Biol.* 5:44-50, 1853.
2. Leyden, E.: Zur Kenntnis des Bronchial-Asthma. *Virchows Arch. f. path. Anat.* 54:324-352, 1872.
3. Böttcher, A.: Farblose Krystalle eines eiweissartigen Körpers aus dem menschlichen Sperma dargestellt. *Virchows Arch. f. path. Anat.* 32:525-535, 1865.
4. Schreiner, P.: Ueber eine neue organische Basis in thierischen Organismen. *Ann. d. Chem.* 194:68-84, 1878.
5. Majert, W., and Schmidt, A.: Ueber das Piperazine (Hoffmann's Diathylendiamin, Landenburg's Aethylenimin, Schreiner's Spermin). *Ber. d. deutsch. chem. Gesellsch.* 23:3718-3726, 1890.
6. White, J. C.: Leukosin. *Boston M. & S. J.* 60:89-94, 1859.
7. Cohn, T.: Beitrag zur Kenntnis des Charcot'schen und Böttcher'schen Krystalle. *Deutsches Arch. f. klin. Med.* 54:515-524, 1895.
8. Schwarz, E.: Die Lehre von der allgemeinen und örtlichen "Eosinophilie." *Ergebn. d. allg. Path. u. path. Anat.* 17:137-789, 1914.
9. Liebreich, E.: *Le sang in vitro: éosinophilie, fibrinogenèse, phagocytose des hématies.* 128 pp. Paris: Masson et Cie., 1921.
10. Neumann, A.: Ueber die Natur der Charcot-Leyden-Böttcher-Neumann Krystalle. *Ztschr. f. physiol. Chem.* 173:69-71, 1927.
11. Wrede, F.; Boldt, F., and Buch, E.: Ueber die Natur der Charcot-Leyden-Böttcher-Neumann Krystalle. *Ztschr. f. physiol. Chem.* 165: 155-166, 1927.
12. Bahrmann, E.: Ueber ein gleichzeitiges Vorkommen von Asthma bronchiale mit rheumatischer eosinophiler Gefässentzündung. *Virchows Arch. f. path. Anat.* 296:277-288, 1935.
13. Thomson, A. P.; Wilson, G. H., and McDonald, S.: Three cases of unusual illness with eosinophilia: one with lesions in the liver resembling those of tularemia. *Lancet* 2:9-13, 1937.
14. Turner, J. C.; Jackson, H., Jr., and Parker, F., Jr.: The etiologic relation of the eosinophil to the Gordon phenomenon in Hodgkin's disease. *Am. J. M. Sc.* 195:27-32, 1938.
15. Oppenheimer, C.: *Handbuch der Biochemie.* Vol. I. 932 pp. Jena: Gustav Fischer, 1909. Pp. 816-818.
16. Poehl, A.: Der Nachweiss des Spermins in verschiedenen Drüsen des thierischen Organismus und die chemische Zusammensetzung des Brown–Séquard'schen Heilmittels. *Deutsche med. Wchnschr.* 18:1125-1128, 1892.
17. Code, C. F., and MacDonald, A. D.: The histamine-like activity of blood. *Lancet* 2:730-733, 1937.
18. Acton, H. W.: The significance of Charcot-Leyden crystals in the faeces as an indication of amoebic colitis. *Indian J. M. Research* 6:157-161, 1918.
19. Floderer, H.: Ueber Charcot-Leydensche Kristalle im Empyemeiter. *Wien. klin. Wchnschr.* 16:276-279, 1903.

REPORT ON MEDICAL PROGRESS

ARTERIAL HYPERTENSION*

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THE pathogenesis of arterial hypertension, so far as the underlying physiologic and morphologic processes are concerned, is fairly well established. The relation of certain types of arterial hypertension to renal ischemia has been demonstrated conclusively through experimentation. There is evidence for the presumption that humoral agents of renal origin cause hypertension. However, the biologic nature of the mechanism operating between renal ischemia and hypertension, although the subject of intense investigation, remains to a large extent obscure, particularly in human diseases. Furthermore, there is still much to be learned in the treatment of hypertensive states.

HYPERTENSION IN MAN

Although many investigators have emphasized the fact that arterial hypertension is but a symptom of derangement of the arteriolar system, physicians persist in basing too-rigid judgments of the state of the arterial system and the prognosis of the patient on single measurements of the arterial pressure taken under different conditions. Robinson and Brucer[1] have analyzed the variations in normal blood pressure in a statistical and clinical study of 11,383 persons. The normal range of pressure is considered as 90 to 120 systolic, and 60 to 80 diastolic. About two thirds of the group had pressures below 125 systolic and 80 diastolic. These investigations demonstrate once more the fact that arterial hypertension should not be considered a disease, and that slight or moderate elevation above the normal range should be interpreted with caution. Ayman and Goldshine[2] rightly point out that the present knowledge of essential hypertension is based on measurements of blood pressure made by physicians, largely in the clinic or office. Hardly any data are available regarding the level of blood pressure obtained during a patient's normal routine of living. For this reason these physicians studied 34 patients with various degrees of essential hypertension, whose blood pressures were recorded over a long period in the clinic and at home. The home readings were taken twice daily for weeks or months by the patient or a member of the household. This study reveals that the home

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systolic and diastolic blood-pressure readings are lower than the clinic readings in all cases of essential hypertension. In 30 per cent of the cases the systolic home blood-pressure readings were 40 or more lower than those in the clinic, and in 24 per cent the diastolic home readings were 20 or more lower. The method of frequent blood-pressure readings caused no neurosis or harm in any patient. Those patients with only slight differences between home and clinic readings had in general comparatively little fluctuation of blood pressure from day to day.

The investigation of the physiologic mechanisms underlying arterial hypertension has been carried farther by Stead and Kunkel,[3] who conclude that the increased peripheral resistance offered by the arteriolar system is distributed in a fairly uniform way throughout the body, including the brain. It is of interest that increased vascular resistance was found also in the minute arterial vessels of the voluntary muscles. In the regulation of the tone of these vessels, nervous influences play little or no role as compared with chemical agents. The inference is that in the vasoconstrictor state of the arterioles of the voluntary muscles, humoral factors must be active.

Hines[4] reports again on his experience with the response of the arterial pressure to the cold-pressor test. He outlines the sources of variation in the responses of subjects with arterial hypertension, and claims that under adequately controlled conditions, the response in the same patient is on the whole uniform. Elevation is relatively more significant in the diastolic than in the systolic pressure. Hines considers that a rise of more than 20 systolic and more than 15 diastolic is indicative of a hypertensive, vasoconstrictor mechanism. In persons with arterial hypertension or "tendency" to hypertension the response to the cold-pressor test is increased as much as two to four times that in normal persons. An increased response was noted also in a group of persons with normal pressure who had had hypertension previously or who showed hypertensive eyeground changes. (It is probable that this increased response, like the increased vasoconstrictor response to psychic, painful or other noxious stimuli, is an expression of increased vasoconstrictor irritability of the vessels.) The results obtained by Miller and Bruger[5] indicate that the cold-pressor test is less reliable as a diagnostic aid. These investigators found that 39 per cent of the normal group and 76 per cent of the group with essential hypertension gave a hyperreactor response. It is interesting that in elderly persons with essential hypertension and evidence of nephrosclerosis, the response to the pressor test was less marked than in younger persons with essential hypertension. Patients with chronic nephritis often had a normal reaction. Thomas and Warthin[6] undertook the study of a cold-pressor test under controlled conditions in normal dogs and in those with renal hypertension. In 90 per cent of the tests on the normal group and in 87 per cent on the animals with hypertension, no pressor reaction of over 22 was observed. (On the basis of the available literature and on the basis of personal experience with this test and with other vasoconstrictor reactions in persons with normal and with elevated arterial pressure, I consider that at best the cold-pressor test has somewhat limited significance and applicability.)

Weiss, Dexter, Parker and Tenney[7] report on a systematic study of the nature of arterial hypertension in pregnancy, with particular reference to the toxemic syndrome of pregnancy (pre-eclampsia and eclampsia). There is considerable confusion about the definition, physiologic and structural changes, pathogenesis and etiology of these conditions. These investigators conclude that evidence of some degree of generalized edema was present in 64 per cent of all normal pregnant women who were studied as controls. The physical and chemical characteristics, the distribution, and the time of onset and of post-partum disappearance of the edema of normal pregnancy are similar to or identical with those of the edema associated with toxemia (pre-eclampsia and eclampsia). At times the generalized edema of normal pregnancy, like that of toxemia, can persist for weeks or months after delivery. In 7 per cent of the normal pregnant women with generalized edema, symptoms such as frontal headaches, visual disturbances, nausea and vomiting — similar to the symptoms seen in toxemia or in severe premenstrual edema — were noted, and in these patients a close relation was found between the cerebral symptoms and the daily appearance, usually in the morning, and disappearance of facial edema. In one patient with severe generalized edema, but with normal blood pressure and no proteinuria, eclamptiform convulsions occurred. The mechanism of the edema of normal pregnancy, like that of pre-eclampsia and eclampsia, could not be explained by any of the usual causes for edema formation. By exclusion, a chemical or hormonal etiology resulting in retention of water and electrolytes in the tissues is suspected.

The same authors emphasize that not all types of hypertension observed in pregnancy should be considered as "toxemia." Prepregnant hypertension uninfluenced by pregnancy and hypertension developing or accentuated during pregnancy should

be differentiated. Only the latter is a phase of toxemia. About half the patients with hypertension of varied etiology before their pregnancy had no aggravation of the hypertensive state during pregnancy, and had no evidence of toxemia. The two most important factors predisposing to pre-eclampsia and eclampsia are prepregnant hypertension and generalized edema. Pyelonephritis and other nephritides predispose to toxemia only so far as they are associated with hypertension and edema. The significance of symptoms and signs of pre-eclampsia and eclampsia is discussed in this report.

From a study of the etiology of toxemia, they conclude that death of the fetus in utero usually does not result in improvement. Following fetal death, hormones originating in the placenta usually continue to be eliminated in the urine, indicating continued activity of the placenta. These workers claim that there is no valid evidence that pressure on the ureter or renal artery is responsible for pre-eclampsia or eclampsia. The conclusion is reached that the presence of a *functioning* placenta maintains the syndrome, and that removal of the placenta is responsible for improvement.

They also state that sustained hypertension follows toxemia in about one third of the patients with normal blood pressure before pregnancy. In these cases toxemia induces permanent "post-toxemic" hypertension. In general the longer the existence of the toxemia, the greater is the tendency to sustained post-partum hypertension. The characteristic morphologic changes of toxemia present in the placenta, kidneys and liver are described. The renal changes consist of a type of glomerulonephrosis. Structural changes in the minute vessels of the kidney can develop within a few weeks in the presence of toxemia. It is concluded that, among the underlying causative factors, chemical substances originating in the placenta are primarily responsible for the syndromes.

Schroeder and Steele[8] have attempted to classify essential hypertension on the basis of the relation of presenting phenomena to renal, nervous, endocrine and vascular symptoms. It is questionable whether this classification is rational or serves a constructive purpose. Williams and Harrison[9] proposed a classification based partly on underlying causative factors and partly on aggravating factors. In this classification, Group I includes hypertension of neurogenic origin; Group II includes cases of endocrine origin; Group III includes cases with renal diseases, such as acute and chronic nephritis, urinary obstructions and renal arterial disease; Group IV includes hypertension of metabolic origin such as hypercholesteremia and gout associated with renal vascular lesions; Group V includes cases of hypertension caused by congestive failure of the heart; and Group VI includes unclassified cases. Weiss,[10] discussing the clinical and physiologic characteristics of arterial hypertension, proposes the following classification of types of clinical hypertension:

I. Hypertension of organic vascular origin, with renal ischemia.
   1. Congenital malformations.
      a. Coarctation of the aorta.
      b. Hypoplastic renal artery.
      c. Polycystic kidneys.
   2. Inflammatory vascular diseases.
      a. Glomerulonephritis.
      b. Pyelonephritis.
      c. Periarteritis nodosa.
      d. "Rheumatic" arteritis.
      e. Disseminated lupus erythematosus.
   3. Degenerative vascular diseases.
      a. Arteriosclerotic occlusive lesions of the renal artery (essential hypertension).
      b. Renal arteriolosclerosis.

II. Hypertension of organic vascular origin, without renal ischemia (diffuse arterial and arteriolar sclerosis).

III. Hypertension of nonorganic vascular origin.
   1. Endocrine disorders.
      a. Pituitary dysfunction and neoplasms (Cushing syndrome).
      b. Adrenal dysfunction and neoplasms (cortical and medullary).
      c. Certain types of toxemia of pregnancy.
   2. Nervous disorders.
      a. Cerebral trauma.
      b. Cerebral neoplasms.
      c. Poliomyelitis.
      d. Rare vascular diseases of the brain.

This classification does not include the secondary factors that accentuate hypertension — that is, emotions, complete heart block, aortic insufficiency and so forth. Carotid-sinus reflexes, bichloride of mercury, lead, tobacco, alcohol, syphilis, hydronephrosis, prostatic obstruction, spinal bladder and infarcts of the kidney are not considered *primary* causative factors of hypertension. So-called "malignant" hypertension is held to be only a special type of severe spastic and structural vascular response, which can develop in any type of hypertension. Although renal ischemia is considered today the most important cause of hypertension, diffuse arterial and arteriolar sclerosis (Group II), irrespective of renal involvement, is still included in this etiologic classification of hypertension. At present it is not known whether in essential hypertension with renal arteriolosclerosis the local degenerative process is a primary process, or whether the

arteriosclerosis is preceded by a renal vasospastic stage caused by humoral agents of renal or extrarenal origin.

Rosenberg[11] has studied the symptoms and the histologic changes in the brains of 17 patients with the malignant type of hypertension. He found the cerebral symptoms in these patients frequently associated with such organic lesions as increased intracranial pressure resulting from cerebral edema, multiple microscopic cerebral lesions and vascular accidents involving the larger vessels.

Stead and Kunkel[12] have investigated the nature of the transient hypertension induced in man by Paredrinol. It is pertinent to note that, in contrast to the hypertension induced by adrenalin or other sympathomimetic drugs, this hypertension is characterized by several factors that are similar to or identical with those observed in spontaneous human hypertension. The cardiac output, circulation time and basal metabolism remain normal. The decrease in the heart rate depends on stimulation of the carotid-sinus reflex. De Wesselow and Thomson[13] have investigated the effect of certain electrolytes particularly sodium and potassium, on the level of the arterial pressure. Variations in the dietary intake of these substances have little or no effect on the level of the arterial pressure. With the administration of unusually large amounts of sodium, the blood pressure rose, whereas an excessive amount of potassium had the opposite effect. The rise apparently depended on increase in blood volume caused by the sodium, and the fall on the effect of potassium on the heart.

Experimental Hypertension of Renal Origin

Experimental investigation of the nature of the interrelation between the kidney and the arterial pressure has continued vigorously. Page[14] has reported one more method of inducing arterial hypertension of renal origin, namely, the use of a cellophane envelope to produce collagenous perinephritis, which in turn causes renal ischemia and hypertension. This hypertension, which is similar to that induced by other forms of renal ischemia, persists after renal denervation but is abolished by bilateral adrenalectomy. Greenwood, Nassim and Taylor[15] considered the possibility that the release of the renal pressor substance was a physiologic response to a disproportion between the work required of the kidney and its available blood supply. If this concept were true, it followed that it should be possible to produce hypertension by preventing the hypertrophy of a kidney that occurs following the removal of the opposite kidney. This was accomplished in dogs by enveloping the remaining kidney with strips of gauze, which were then soaked with collodion and allowed to harden, a layer at a time, in situ. Such application of a cast to one kidney followed by extirpation of the opposite one is a reliable method of producing a pronounced and rapid rise in blood pressure. It is not clear, however, that the prevention of renal hypertrophy or active constriction of the kidney or its vessels is the active causative agent in these experiments.

Goldblatt, Kahn and Hanzel[16] have studied the effect of constriction of the abdominal aorta above and below the origin of the renal arteries, and have concluded that the hypertension developing after constriction of the aorta above the origin of the renal arteries is of renal etiology. The findings of Page[17] confirm this. Hypertension does not develop in dogs, however, if the aorta is constricted or occluded at the arch, a situation corresponding to that existing in man in the presence of coarctation of the aorta, a condition which is accompanied by hypertension. This difference is explained by the fact that in the dog extensive collateral circulation develops rapidly and with ease.

Taquini[18] reports that on re-establishing the renal circulation after temporary occlusion of the renal arteries there is a rise in the arterial pressure. This hypertension is caused presumably by the liberation of a substance, formed in the totally ischemic kidney, that acts on the walls of the vessels throughout the body.

Significance should be attached to the publication of several reports on the biologic and chemical characteristics of the vasopressor and the vasodepressor substances of renal origin. Corcoran and Page[19] have found that renin (the vasoconstrictor substance extracted from the kidney of certain animals), when given slowly by intravenous injection to uninephrectomized dogs whose remaining kidney has been subcutaneously explanted, increases the systemic arterial pressure and the relative volume of renal glomerular filtrate while it decreases renal blood flow. The investigators suggest that this reduction of the blood flow depends on the constrictor effect of renin on the glomerular efferent arterioles. However, under different experimental conditions Steele and Schroeder[20] usually failed to observe any change in the renal blood flow following a single intravenous administration of renin. Subsequently Corcoran and Page[21] reinvestigated this problem and found that the results substantiated their first conclusion that slow intravenous infusion of renin into uninephrectomized dogs with single explanted kidneys caused a decreased renal blood flow.

Page[22] observed that after repeated injection of renin, a diminishing pressure response (tachyphylaxis) occurred in cats and dogs, even after the re-

moval of the liver, adrenal glands, kidneys or viscera. The pressor response to renin in brief experiments is independent of the height of the arterial pressure or of the presence of the adrenal glands. Evisceration and large doses of ergotamine reduce the response. The effect is largely uninfluenced by pithing, the intracisternal injection of renin, cocaine, strychnine and caffeine and the infusion of sodium bicarbonate or hydrochloric acid. No parallel was found between the pressor responses to renin on the one hand and to carotid-sinus stimulation, adrenalin and tyramine on the other. For a time, continuous infusion of renin produces a prolonged rise of arterial pressure in normal and in chronically adrenalectomized dogs, but eventually the pressure falls even though the injection is continued. Tachyphylaxis can develop in a rabbit's ear perfused with blood and small doses of renin, and the same blood perfused through a second ear will cause no vasoconstriction when renin is added. The addition of renin-activator restores the ability of renin to cause constriction. Renin alone causes no vasoconstriction when infused with Ringer's solution, but here again renin-activator restores activity. It is suggested that the diminishing pressor response observed in animals after repeated injection of purified renin is due to the loss of renin-activator and to the development of an "antisubstance" in the blood. The vasoconstrictor effect of renin and renin-activator depends primarily on direct action on the blood vessels and is little influenced, at least in experiments of short duration, by the removal of the nervous system, endocrine glands and viscera. Page and Helmer[23] reported later on the chemical action of a crystalline pressor substance ("angiotonin") derived from the reaction between renin and renin-activator. The vasoconstrictor activity of purified renin can be restored by the addition of a protein-like substance contained in plasma and red blood cells (renin-activator). The activated renin, angiotonin, is a heat-stable, water-soluble, alcohol-soluble, fluorescent, and alkaline-labile substance. It is a reducing substance that is destroyed by strong oxidizing agents. It forms crystalline salts with oxalic and picric acids. Maximal amounts of angiotonin result when the proportion between renin and activator is roughly 3:100. Renin destroys angiotonin when incubated with it for a sufficient length of time. Angiotonin also has an activator — apparently different from the renin-activator — that can be separated from blood.

The purest preparation of renin elevates the arterial pressure 30 mm. of mercury in dogs, when injected in amounts representing 0.027 mg. of nitrogen per kilogram of body weight. In cats it was three times as active. Color tests for guanidine groups and for pentose are especially strong in renin solutions; those for adrenaline are negative. Crystalline precipitates are formed by the addition of flavianic acid or picric acid to hydrolysates of renin. The pressor action of renin in cats and dogs is not abolished by ergotamine, nor potentiated by cocaine as is adrenaline. Cats, under Pentobarbital, are desirable animals for assay purposes.

Page and Helmer state that angiotonin causes marked contraction of intestinal segments of rabbits without reducing their rhythmic motion. It sensitizes the intestine to further doses of angiotonin and alters the intestine so that renin-activator contracts it. Angiotonin also constricts the vessels of a rabbit's ear perfused with blood or Ringer's solution. The kidneys form inhibitors to both renin and angiotonin.

Page[24] subsequently reported on the amount of renin, renin-activator and angiotonin-activator in the renal vein and in the arterial blood. Heparinized plasma derived from the blood of some patients with essential hypertension causes greater renin-activation than does normal human blood. Plasma from dogs with experimental hypertension also exhibits heightened power as compared with plasma of normal dogs. This, according to Page, suggests that the humoral mechanism in the two types of hypertension have much in common, and that in the hypertensive state there is either an increased amount of renin-activator in the blood or a decreased amount of renin-inhibitor.

Braun-Menendez, Fasciolo, Leloir and Munoz[25] report on the nature of the substance causing renal hypertension. Extracts of the venous blood from kidneys in acute ischemia contain a pressor substance ("hypertensin") that is also formed in vitro when blood proteins are incubated with renin. Some of the chemical and pharmacologic properties of hypertensin differ from those of other known substances. Renin is considered the enzyme, blood pseudoglobulins the substrate, and hypertensin the reaction product. Hypertensin disappears if the reaction is permitted to go too far, and is also inactivated by other proteolytic enzymes and by blood. The pressor action of renin appears to be due to the formation of hypertensin in blood, and a similar mechanism is suggested for arterial hypertension due to renal ischemia.

Pickering and Prinzmetal[26] report on the nature of diuresis induced in the rabbit by renin. The intravenous dose of renin necessary to produce diuresis in the anesthetized rabbit is greater than that needed to produce a rise in arterial pressure. In

the unanesthetized rabbit under special experimental conditions, renin can have an antidiuretic effect, which is attributed to its action on the glomerular vessels in reducing the rate of glomerular filtration. The diuretic effect of renin in the unanesthetized rabbit is due to an inhibition of tubular reabsorption of water, sodium and chloride. This may represent the effect of a pressure diuresis in which relatively few nephrons are involved, but it is more probably due in part to the direct action of renin on the function of the renal tubule cells.

Williams, Grollman and Harrison[27] found that an extract of the kidney, administered before the renin, diminished its pressor effect, and that such extracts also reduced the blood pressure of rats with hypertension due to removal of renal tissue. Likewise, in hypertensive dogs treated with renal extracts, the blood pressure was appreciably reduced, normal values being attained in some cases. Oral administration of extracts to normal animals did not produce a decline in blood pressure. Unless the hypertension was mild, several untoward symptoms and even death were associated with the decline of pressure. Grollman, Williams and Harrison[28] have treated a small number of patients by means of oral or parenteral administration of the renal antipressor substance. In most of the subjects, it is claimed, a decline in the blood pressure occurred. The renal antipressor substance apparently has certain unique properties that differentiate it from various depressor tissue extractives described previously by investigators. This depressor substance is still very costly and difficult to obtain. In the discussion of the above reports Winternitz[29] stated that the crude ammonium sulfate preparation of renin contains pressor and depressor substances, as well as agents that necrotize certain muscles, including the heart muscle, the smooth muscles of the arteries, veins and other hollow muscular viscera, and diaphragmatic but not skeletal muscle. Renin D, according to Winternitz, contains three ferments: a tryptic, a peptic and a catalytic type. At the same meeting Jablons[30] reported that he had treated hypertensive animals and patients with a hypotensive, protein-free, aqueous, acid-alcohol extract. Some of the patients reacted well, whereas others were not benefited.

The interpretation of these results bearing on the nature of pressor and depressor substances and on their biologic significance in disease is difficult.

Treatment

There has been no significant progress in the treatment of arterial hypertension and its complications. However, advances in the knowledge of the pathogenesis and treatment of pyelonephritis bear significantly on the prevention of hypertension due to chronic or healed pyelonephritis. Similarly the demonstration that within a period of weeks toxemia of pregnancy can induce structural changes in the renal vessels suggests that the timely interruption of toxemic pregnancies will reduce the tendency to post-toxemic arterial hypertension.

The present status of the treatment of arterial hypertension and its complications, including a review of the recent literature on the subject, I[31] have discussed elsewhere. It has been pointed out that a diet low in sodium (salt) is neither practical nor very effective in the treatment of essential hypertension or hypertension caused by chronic pyelonephritis. In the toxemias of pregnancy (preeclampsia and eclampsia) and in many cases of acute or subacute glomerulonephritis, on the other hand, a low-sodium intake not only improves the degree of edema, but also lowers the arterial pressure. Recently, by claiming the regime efficacious, Martini[32] and Kampmann[33] revived the interest in a rigid salt-free diet combined with periodic fasting in the treatment of arterial hypertension. The initiation of the fasting period is preceded by a saline laxative. During the eight days of fasting usually about 750 cc. of fruit juices or tomato juice are given daily. One cup of tea or a small amount of fresh fruit or salad may be added. No other fluids are allowed. About three days after the end of the strict fasting period the patient returns to the salt-free diet. During the transition period, potato, vegetables, salads and applesauce are added to the diet. The report suggests that this strict diet is not without danger. It should be carefully supervised in old persons, and in the presence of severe heart failure and myocardial infarction it is contraindicated. Depression, nervousness and weakness have occurred in some patients on this regime. A tendency to circulatory collapse developed in others.

The use of the depressor substance of renal origin, as recommended by Grollman, Williams, and Harrison,[28] is still in the experimental stage, and the drug is both costly and difficult to obtain. For these reasons it is too early to express an opinion on the drug's significance from a therapeutic point of view.

The therapeutic value of neurosurgical procedures is still an unsettled question. Smithwick[34] reports on his surgical experience in approximately 150 cases of hypertension. He believes that sympathectomy yields its best result when the operation is adequately complete, preganglionic in type and extensive enough to guard against future regeneration of interrupted pathways. If the splanch-

nic area was thoroughly denervated, an immediate postural change in blood pressure resulted in every case. Under these circumstances the blood-pressure level in all positions and the pulse pressure were lower than before operation. If splanchnic denervation is less complete, and if no significant postural change is noted, there is usually no significant change in the blood-pressure level in any position, particularly in the more advanced stages of the disease. Apparently, a few uninterrupted fibers are capable of supplying enough tone to the splanchnic area so that no significant change will occur in blood pressure after operation.

According to Smithwick, removal of virtually the entire great splanchnic nerve and division of all its aortic branches, coupled with interruption of the communicating rami of the ninth, tenth, eleventh and twelfth dorsal and first lumbar segments, and with excision of the sympathetic trunk over this area, constitute the minimal procedure that has been found consistently to produce the blood-pressure change described above. Whether removal of the outflow from the second lumbar segment is also desirable has not been determined. Smithwick considers his contribution as a preliminary report, and he emphasizes that it will take several years to ascertain the value of this procedure in the treatment of hypertension.

If one recalls the number of claims and counterclaims as to the efficacy of the numerous types of neurosurgical procedures ever since Pieri[35] in 1932 resected both splanchnic nerves in patients with essential hypertension, one wonders about the effectiveness of these measures. Volini and Flaxman,[36] impressed by the observation that the majority of proposed therapeutic measures have a brief popularity and then pass into obscurity, undertook a comparative evaluation of the results of nonspecific surgical measures (hysterectomy, cholecystectomy and prostatectomy) and of specific neurosurgical operations (extensive sympathectomy, splanchnic nerve resection and celiac ganglionectomy). The authors followed the effects of fifty-two operations on hypertensive patients and concluded that any of the claims made for the efficacy of specific operations can likewise be made for nonspecific surgical measures. Obviously, then, the value of neurosurgical treatment of hypertension is not yet established.

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References

1. Robinson, S. C., and Brucer, M.: Range of normal blood pressure: statistical and clinical study of 11,383 persons. *Arch. Int. Med.* **64**:409-444, 1939.
2. Ayman, D., and Goldshine, A. D.: Blood pressure determinations by patients with essential hypertension. *Am. J. M. Sc.* **200**:465-474, 1940.
3. Stead, E. A., Jr., and Kunkel, P.: The nature of peripheral resistance in arterial hypertension. *J. Clin. Investigation* **19**:25-33, 1940.
4. Hines, E. A., Jr.: The significance of vascular hyperreaction as measured by the cold-pressor test. *Am. Heart J.* **19**:408-416, 1940.
5. Miller, J. H., and Bruger, M.: The cold-pressor reaction in normal subjects and in patients with primary (essential) and secondary (renal) hypertension. *Am. Heart J.* **18**:329-333, 1939.
6. Thomas, C. B., and Warthin, T. A.: The response of normal dogs and dogs with experimental hypertension to a standard cold stimulus. *Am. Heart J.* **19**:316-329, 1940.
7. Weiss, S.; Dexter, L.; Parker, F., Jr., and Tenney, B., Jr.: Arterial hypertension in pregnancy and the hypertensive toxemia syndrome of pregnancy (preëclampsia and eclampsia). *Tr. A. Am. Physicians* **55**:282-288, 1940.
8. Schroeder, H. A., and Steele, J. M.: Studies on "essential" hypertension. I. Classification. *Arch. Int. Med.* **64**:927-951, 1939.
9. Williams, J. R., Jr., and Harrison, T. R.: Clinical pictures associated with increased blood pressure: a study of one hundred patients. *Ann. Int. Med.* **13**:650-670, 1939.
10. Weiss, S.: The clinical and physiologic characteristics of arterial hypertension. *Blood Heart and Circulation*. Edited by Forest R. Moulton. 331 pp. Washington: American Association for the Advancement of Science. 1940. P. 300.
11. Rosenberg, E. F.: The brain in malignant hypertension: a clinicopathologic study. *Arch. Int. Med.* **65**:545-586, 1940.
12. Stead, E. A., Jr., and Kunkel, P.: Mechanism of arterial hypertension induced by Paredrinol (*a*-N-dimethyl-*p*-hydroxyphenethylamine). *J. Clin. Investigation* **18**:439-448, 1939.
13. De Wesselow, O. L. V. S., and Thomson, W. A. R.: A study of some serum electrolytes in hypertension. *Quart. J. Med.* **8**:361-374, 1939.
14. Page, I. H.: The production of persistent arterial hypertension by cellophane perinephritis. *J. A. M. A.* **113**:2046-2048, 1939.
15. Greenwood, W. F.; Nassim, R., and Taylor, N. B.: The production of hypertension by the prevention of kidney hypertrophy. *Canad. M. A. J.* **41**:343-345, 1939.
16. Goldblatt, H.; Kahn, J. R., and Hanzel, R. F.: Studies on experimental hypertension. XI. The effect on blood pressure of constriction of the abdominal aorta above and below the site of origin of both main renal arteries. *J. Exper. Med.* **69**:649-674, 1939.
17. Page, I. H.: The effect of chronic constriction of the aorta on arterial blood pressure in dogs: an attempt to produce coarctation of the aorta. *Am. Heart J.* **19**:218-232, 1940.
18. Taquini, A. C.: The production of a pressor substance by the totally ischemic kidney. *Am. Heart J.* **19**:513-518, 1940.
19. Corcoran, A. C., and Page, I. H.: The effects of renin on renal blood flow and glomerular filtration. *Am. J. Physiol.* **129**:698-702, 1940.
20. Steele, J. M., and Schroeder, H. A.: Effect of renal extract (renin) upon the flow of blood through various organs. *J. Clin. Investigation* **18**:477, 1939.
21. Corcoran, A. C., and Page, I. H.: Effects of renin, pitressin, and pitressin and atropine on renal blood flow and clearance. *Am. J. Physiol.* **126**:354-367, 1939.
22. Page, I. H.: On the nature of pressor action of renin. *J. Exper. Med.* **70**:521-533, 1939.
23. Page, I. H., and Helmer, O. M.: Crystalline pressor substance (angiotonin) resulting from the reaction between renin and renin-activator. *J. Exper. Med.* **71**:29-42, 1940.
    Helmer, O. M., and Page, I. H.: Purification and some properties of renin. *J. Biol. Chem.* **127**:757-763, 1939.
24. Page, I. H.: Demonstration of the liberation of renin into the blood stream from kidneys of animals made hypertensive by cellophane perinephritis. *Am. J. Physiol.* **130**:22-28, 1940. Difference in the activating effect of normal and hypertensive plasma on intestinal segments treated with renin. *Ibid.* **130**:29-33, 1940.
25. Braun-Menendez, E.; Fasciolo, J. C.; Leloir, L. F., and Munoz, J. M.: The substance causing renal hypertension. *J. Physiol.* **98**:283-298, 1940.
26. Pickering, G. W., and Prinzmetal, M.: The effect of renin on urine formation. *J. Physiol.* **98**:314-335, 1940.
    Harrison, T. R.; Grollman, A., and Williams, J. R., Jr.: The antipressor action of renal extracts and their capacity to reduce the blood pressure of hypertensive rats. *Am. J. Physiol.* **128**:716-724, 1940.
27. Williams, J. R., Jr.; Grollman, A., and Harrison, T. R.: The reduction of the blood pressure of hypertensive dogs by the administration of renal extract. *Am. J. Physiol.* **130**:496-502, 1940.
28. Grollman, A.; Williams, J. R., Jr., and Harrison, T. R.: Reduction of elevated blood pressure by administration of renal extracts. *J. A. M. A.* **115**:1169-1176, 1940.
29. Winternitz, M. C.: discussion of Grollman, Williams and Harrison.[28]
30. Jablons, B.: discussion of Grollman, Williams and Harrison.[28]
31. Weiss, S.: Arterial hypertension and its complications. In *Modern Medical Therapy in General Practice*. Edited by David P. Barr. Vol. III. 1116 pp. Baltimore: Williams & Wilkins Co., 1940. Pp. 2711-2749. Diet and Bright's disease. *Connecticut State M. J.* (in press).
32. Martini, P.: Ueber die Behandlungsmöglichkeiten des genuinen Hochdrucks, insbesondere über salzfreie Ernährung. *München. med. Wchnschr.* **85**:1409-1414, 1938.
33. Kampmann, W.: Ueber die Behandlungsmöglichkeiten des Hochdrucks, insbesondere über das Fasten. *Deutsches Arch. f. klin. Med.* **184**:216-243, 1939.
34. Smithwick, R. H.: A technique for splanchnic resection for hypertension. *Surgery* **7**:1-8, 1940.
35. Pieri, G.: Tentativi di cura chirurgica dell'ipertensione arteriosa essenziale. *Riforma med.* **48**:1173-1180, 1932.
36. Volini, I. F., and Flaxman, N.: The effect of nonspecific operations on essential hypertension. *J. A. M. A.* **112**:2126-2128, 1939.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26491

PRESENTATION OF CASE

A fifty-six-year-old housewife entered the hospital complaining of pain and swelling of the right leg.

Three years before admission the patient first noticed a slight stiffness and swelling of the right ankle that was aggravated by walking or standing for a long time and alleviated by a night's rest. Two years before admission a constant pain was added to these symptoms. It was situated over the dorsum of the tarsus, gradually increased in severity and was accompanied by an increase in swelling of the ankle joint. Her physician treated the joint for strain and "rheumatism," and ten months before admission another physician made a diagnosis of arthritis. Nine months before admission the patient entered another hospital, where x-ray examination showed that the cortex of the lower end of the right tibia was destroyed, without expansion. Five weeks later there was progression of the destruction, with definite evidence of new-bone formation, but no expansion of the cortex and no apparent infiltration of the lesion into the soft parts. A biopsy was reported as showing osteomyelitis. Films taken two and five months later showed no change. The patient remained in bed for the next six weeks and was then able to use crutches, but pain and swelling returned and forced her to remain in bed almost constantly. The biopsy wound drained for four months, and five months before admission the ankle joint became fixed. The patient entered this hospital because of increasing pain and swelling of the joint. She had lost 15 pounds in the two years prior to entry and had had nocturia two or three times a night.

In the past the patient had the usual childhood diseases. Twenty years before admission she sprained the right ankle, and twelve years before admission fractured the right fibula. Her mother had died of pneumonia, one sibling of cancer of the stomach, and two siblings of tuberculosis.

Physical examination showed a well-developed and well-nourished woman in no apparent distress. The breasts were normal to palpation. Examination of the heart, lungs and abdomen was negative; the blood pressure was 142 systolic, 74 diastolic. There was a 2.5-cm. shortening of the right tibia. The swollen right ankle was almost 5 cm. greater in circumference than the left, and the joint was held in 20° equinus. There was a fusiform swelling of the middle third of the tibia, and a 10-cm. scar three fingerbreadths above the medial malleolus, with a healed sinus in its center. The calcaneus was inverted 15°, and the lower end of the tibia projected forward. An increase in temperature was noted in the lower two thirds of the leg, with diffuse tenderness, most marked over the malleoli. The ankle showed slight pitting edema, but no fluctuation. Very slight painless motion was present in the midtarsal, subastragaloid and ankle joints. An extremely painful lateral motion could be elicited in the tibia 7.5 cm. above the medial malleolus. An area of roughening was present in the midshaft of the tibia. The right thigh was somewhat atrophic. There was no lymphadenopathy or tenderness along the lymphatic vessels draining the part.

The temperature was 99.5°F., the pulse 85, and the respirations 20.

The urine showed a negative to ++ test for albumin, with a few white and red blood cells per high-power field. Examination of the blood showed a red-cell count of 4,590,000 with a hemoglobin of 80 per cent, and a white-cell count of 8900 with 64 per cent polymorphonuclears. The blood calcium was 10.8 mg. per 100 cc., the phosphorus 3.5 mg., and the phosphatase 3.3 units. The blood Hinton and gonococcal fixation tests were negative.

X-ray films of the right foot and foreleg showed extensive destruction of the lower end of the tibia, involving the joint surface. The cortex was fractured in several places, and a number of sequestrums were present. A small amount of new-bone formation was seen in the upper aspect of the area of destruction posteriorly. Mottled decalcification involved the adjacent portion of the tibia and extended upward for at least another 18 cm. There was some periosteal new-bone formation in this area. An apparent pressure defect involved the lower end of the fibula. There was a fairly well-circumscribed soft-tissue mass in the anterior aspect of the large area of destruction in the lower end of the tibia and some edema higher up in the tibia. There were marked decalcification of the bones of the foot and a small area of calcification in the soft tissues below the medial malleolus.

Films of the knee joints showed marked decalcification about the lower end of the femur and the upper end of the tibia and fibula on the right side. There was no definite evidence of bone destruction close to the knee joint. There was

marked atrophy of the muscles of the right leg. The skull and pelvis showed no evidence of disease.

Chest plates showed extensive calcification in the left-lower-lung field, part of which could have been in the pleura. There was hilar calcification, and some calcification at the right base. No evidence of metastases was observed.

On the eighteenth hospital day, an operation was performed.

Differential Diagnosis

Dr. Channing C. Simmons: A fifty-six-year-old woman entered this hospital complaining of stiffness and swelling of the ankle of three years' duration. At first the pain was relieved by rest, and she was treated for "rheumatism." She had entered another hospital nine months previously, when x-ray study showed bone disease; a biopsy was performed and the specimen was reported as showing osteomyelitis. The symptoms were not relieved, and she was finally admitted to this hospital. Twelve years previously, she had injured the right ankle. Examination of the heart and lungs was negative. There were a tumor at the lower end of the tibia and a 10-cm. scar, with some limitation of motion of the ankle. The other bones were normal except for atrophy. The temperature was slightly elevated, but examination of the urine and blood was negative. The chemical constituents of the blood were normal, although a serum protein test was not made.

We should have a certain amount of additional information, particularly a more extensive past history and a more detailed physical examination. I should like to know whether there was any evidence of tumor elsewhere in the body, namely, in the breast, pelvis, thyroid gland or genitourinary tract, and whether the serum protein was elevated. Sometimes it is valuable to perform a spinal-fluid Wassermann test. We should probably discount the pathological report of osteomyelitis. I do not mean to say that she did not have it, but that it was probably a secondary condition superimposed on some other process. There was a destructive process of the lower 7.5 cm. of the tibia, with some new-bone formation above. It did not extend into the ankle joint. In this film one can also see small areas of rarefaction in the upper end of the tibia and in the lower femur.

We should consider some form of bone tumor. Osteogenic sarcoma is the first thing that comes to one's mind. In a woman over fifty, it is rare except in the presence of Paget's disease. The phosphatase was normal. One would expect it to be high in Paget's disease. Ewing's sarcoma is unusual in a woman of this age, and is generally in the shaft rather than in the lower end of the bone. I do not see how we can rule out reticulum-cell sarcoma, although the duration is long for this kind of tumor. It is a bone-destructive process, with relatively little new-bone formation, and may be of slow or rapid growth. Syphilis must be considered, because it can cause the picture of any bone disease. The same thing is true of lymphoma. Plasma-cell myeloma is usually multiple, occasionally single, but one would expect the serum protein to be higher. Although the findings are not characteristic of plasma-cell myeloma, the possibility must be considered. Another possible bone tumor is a metastasis from a primary lesion elsewhere. Since the breasts were presumably normal, thyroid carcinoma, hypernephroma and neuroblastoma should be especially considered.

An inflammatory condition does not seem likely with the white-cell count and temperature noted in this patient, and in tuberculosis one would expect involvement of the joint.

Metastases from a primary tumor are apt to occur more readily at a point of injury, in other words where one receives a blow; hence a cancer of the breast, if it metastasizes, is more apt to appear at the site of a previous injury than elsewhere. The same thing presumably holds true in a fracture of an ankle. This is probably not an inflammatory condition. My first choice is metastatic tumor from some site unknown, and my second an osteogenic sarcoma; a myeloma is a possibility.

A Physician: What is the relation of injury to primary tumor in that region?

Dr. Simmons: That opens up a controversial subject. In the Registry of Bone Sarcoma, 40 per cent of the cases give a definite history of trauma, the tumor following relatively soon; hence with sarcoma there is some relation to injury. The general belief is that carcinoma is not caused by a single blow.

Dr. James R. Lingley: The x-ray films show an extensive destructive lesion involving the lower extremity of the tibia and extending up the shaft for a considerable distance. There is some periosteal, new-bone formation, and there is a large soft-tissue mass surrounding the lesion. The appearance is very much in favor of tumor rather than infection. There is no edema of the soft tissues, as one would expect if it were an infectious process. Metastatic tumor could produce the picture. However, it could also be a primary tumor —a primary osteogenic sarcoma, a reticulum-cell sarcoma or a lymphoma.

Clinical Diagnosis

Osteomyelitis of the tibia.

Dr. Simmons's Diagnosis

Metastatic tumor?
Osteogenic sarcoma?

Anatomical Diagnosis

Osteogenic sarcoma of the tibia.

Pathological Discussion

Dr. Tracy B. Mallory: The differential diagnosis on the ward was essentially the same as that of Dr. Simmons. They felt that the odds were against an inflammatory lesion and in favor of tumor. They were not very anxious to commit themselves as to the nature of the tumor.

She was explored and a tumor found, and an amputation was performed. The tumor was a spindle-cell sarcoma producing very little bone, but I think one has to classify it either as an osteogenic sarcoma or a periosteal fibrosarcoma. The extensive bone destruction, the new-bone formation, albeit slight, and the numerous tumor giant cells incline me to the diagnosis of osteogenic sarcoma, however. It certainly is not a reticulum-cell sarcoma. The tumor had destroyed almost the whole lower third of the tibia. It had extended down to the cartilaginous plate at the lower end but had not broken through, the latter remaining as a firm shell between the tumor and the joint. The tumor spread out into the surrounding soft tissues and completely encapsulated the tibia.

CASE 26492

Presentation of Case

A seventy-year-old single woman entered the hospital after coughing or vomiting a large quantity of blood.

Because of the patient's disorientation, the history was obtained from relatives. It appeared that she had been short of breath for a number of years, and four months before admission had spent ten weeks in another hospital because of a coronary occlusion. Following this incident she developed pleurisy, but no details of this illness could be obtained. For some years the patient had suffered from indigestion and for several months before entry had complained of many vague pains, including one in the abdomen that was unrelated to food or activity, but was accompanied by anorexia. Her physician had treated these symptoms with sedatives. During the two weeks prior to entry, she had been disorientated, and it was noticed that her stools were tarry. One week later she developed a nonproductive cough, and four days later swelling of the ankles. On the day of admission she brought up a mouthful of bright-red blood and on two occasions, shortly afterward, dark blood clots. The patient had been losing weight for a year and in the last few weeks before entry had "seemed to melt away."

The patient had had "three nervous breakdowns" in her youth. One brother had died of cancer of the prostate.

Physical examination showed an undernourished, frail woman, who appeared acutely and chronically ill. She lay moaning and muttering and was considerably disorientated. The skin was pale, dry and wrinkled; small, soft lymph nodes could be felt in the neck and axillas; the breasts were normal. Respirations were rapid and shallow, but the lungs were clear. The heart was slightly enlarged and regular, with a loud systolic murmur over the entire precordium; the blood pressure was 116 systolic, 60 diastolic. The abdomen was tense, but no masses or viscera were palpated. Rectal examination was negative; the vaginal introitus was virginal. There was pitting edema of the ankles, and slight varicosities of the legs.

The temperature was 98°F., the pulse 100, and the respirations 20.

Examination of the urine was negative. Examination of the blood showed a red-cell count of 3,500,000 with a hemoglobin of 52 per cent, and a white-cell count of 7900. There was a marked variation in size and shape of the red cells. The nonprotein nitrogen of the blood serum was 26 mg. per 100 cc., the protein 4.5 gm., the carbon dioxide combining power 26.9 milliequiv. per liter, and the chlorides 101.8 milliequiv. Five stool examinations were tarry and guaiac positive.

X-ray examination of the chest showed the left diaphragm to be slightly higher than usual, with clear costophrenic angles. The heart was enlarged on both sides; the aorta was tortuous, dilated and calcified. The bones showed a generalized decalcification. With a gastrointestinal series the esophagus appeared normal, and the stomach contained a moderate amount of foreign material that could possibly have been blood. There were no gross filling defects or ulcerations, and the duodenum showed no evidence of disease. There was extensive calcification in the abdominal aorta.

An electrocardiographic recording showed normal rhythm, a low T_1, diphasic T_2 and T_3, a mostly inverted and diphasic T_4, and a probably absent R_4. The PR interval was 0.12 second.

The patient was put on a gastric diet, and vomiting did not recur until the sixth hospital day,

when it was associated with epigastric tenderness. The vomitus did not contain blood. The lungs were clear. Three days later, 50 cc. of green guaiac-negative fluid was removed from the stomach, and the pain and distention that had developed were relieved by an enema. The patient complained continually of abdominal pain, but examination never revealed more than a generalized tenderness. There was no spasticity. Despite supportive measures, including one transfusion of 500 cc. of blood, the patient failed rapidly and died two weeks after admission.

Differential Diagnosis

Dr. Allen G. Brailey: The patient was already so sick when she reached the hospital that it was not possible to get really adequate information about her. The history is incomplete and may be inaccurate; several laboratory studies would probably have been done if her condition had been more satisfactory. In trying to decide what was the cause of death, let us first consider what kind of illness she had, whether acute or chronic.

We are told that for several years she had had indigestion and shortness of breath; for one year she had been losing weight; for a few months she had had abdominal pain and anorexia; for two weeks she had had tarry stools; and in the hospital she failed rapidly. In other words, she seems to have had a chronic illness that began rather vaguely several months before admission, steadily gaining momentum to the time of its termination. To be sure, it was punctuated by episodes such as the coronary occlusion and the attack of pleurisy, which I assume to have been due to an embolus dislodged from the right ventricular wall. But there is little suggestion in this history of the dramatic change of events that characterizes acute disease.

We may approach this problem from another angle and ask where the disease process was located. We may mention the urinary tract only to rule it out. The nonprotein nitrogen was 26 mg. per 100 cc., and we have the laconic statement that the urine was normal. In fact none of the evidence implicates the kidneys or bladder. Similarly, the respiratory tree seems a most unlikely locus. It is possible to swallow a good deal of bronchial secretion. Indeed, in pulmonary tuberculosis, examination of the stomach contents often yields more tubercle bacilli than does the sputum. But this patient could not have swallowed enough blood from the lungs to produce tarry stools for two weeks. Can the disease process have been primary in the cardiovascular system? The arteries were certainly very sclerotic, as evidenced by the x-ray picture of the aorta, by the history of coronary occlusion and by her mental status, which I assume was due to arteriosclerosis of the cerebral vessels aggravated by anemia. Could the hemorrhage have arisen from rupture of an aneurysm into the gastrointestinal tract? The abdominal pain, perhaps, ought to raise the question of dissecting aneurysm. But the pain was too mild; it lasted too long; and no evidence developed of the arterial shutoff to kidneys or legs that is common in dissecting aneurysm of the aorta. Dissecting aneurysm is preceded by hypertension. This woman might well have had hypertension before the cardiac infarction, but she probably had had little since. I should think that dissecting aneurysm would rarely occur after one's blood pressure has been lowered by any such myocardial injury. There can be little doubt that the fatal disease lay in the gastrointestinal tract.

Dr. Aubrey O. Hampton: They apparently were not very interested in this patient's stomach or duodenum, as judged from the number of films that were taken and from the report. Apparently it was a routine, negative fluoroscopy. They did look for varices in the esophagus and did not find them. In examining the stomach they were handicapped by what was presumed to be foreign material. If these filling defects moved, they were foreign material; but if they did not, they might have been due to a tumor. I do not see any evidence of tumor here.

These shadows near the fundus look like enlarged mucosal folds, and in an elderly woman with cachexia and without hypertension, the folds should be small and atrophic.

She did have an enlarged heart. This is not the true size, however, since this is a portable or "back-to" film, and the size of the heart and aorta is exaggerated.

Dr. Brailey: Do you think the duodenum was all right?

Dr. Hampton: This is a normal-looking duodenal cap. The abdominal aorta shows extensive calcification all the way; it is not dilated.

Dr. Brailey: Did she bleed from esophageal varices? The negative x-ray examination does not exclude that possibility. But we have no evidence of hepatic cirrhosis, and the blood smear is that of long-standing anemia, which, if due to hemorrhage, must be caused by chronic rather than acute blood loss. The hemorrhage from varices is apt to be a succession of acute and widely spaced blood lettings. Could the blood have come from below the duodenum? In the literature there are reports of reverse peristalsis so violent that enemas

had to be stopped because the patient complained of the taste of the enema fluid, but such reversal of flow is uncommon except in intestinal obstruction. On the day of admission the patient brought up bright-red blood that could hardly have come from much below the stomach. The diagnosis that best fits this history is carcinoma of the stomach, with hemorrhage therefrom.

Dr. William B. Breed: Dr. Hampton, from the x-ray films are you willing to make a diagnosis of hypertrophic gastritis?

Dr. Hampton: No. I am assuming that the irregularities were due to large folds that are inadequately demonstrated. To be sure that they are present, one must fluoroscope the patient. These defects are the only abnormal finding I can see in the films that we have.

Dr. Breed: We know that hypertrophic gastritis may give massive bleeding such as this. I do not believe it can be entirely excluded.

Dr. Brailey: I thought about gastritis. The patient was very sclerotic, and the symptoms and downhill course could have been due to senility and circulatory changes in the stomach. But it is a quite impressive picture of rapidly advancing cachexia, which I think was more likely due to cancer than to old age and gastritis.

Clinical Diagnoses

Carcinoma of the stomach.
Coronary heart disease.

Dr. Brailey's Diagnosis

Carcinoma of the stomach.

Anatomical Diagnoses

Acute gastritis.
Arteriosclerosis, generalized.
Coronary occlusion, old.
Infarct of the heart, healed.
Pulmonary infarcts.
Thrombosis, left popliteal vein.

Pathological Discussion

Dr. Tracy B. Mallory: The post-mortem examination showed an area — about 6 cm. in diameter — of very shallow erosion and hemorrhage in the stomach that we must call acute gastritis, although certainly not a hypertrophic gastritis, because the rugae were thin rather than thick. There was nothing else in the gastrointestinal tract. There were severe generalized arteriosclerosis, including the coronary arteries, and an old infarct of the heart in the left ventricle, with an overlying thrombosis. There was an infarct in the lung, and the source of the embolus, as in probably nine out of ten cases, was an unsuspected thrombosis in the popliteal vein.

The brain showed atrophy and rather diffuse arteriosclerosis of the vessels at the base, but no visible or palpable areas of softening. I do not think we can make out a case here for Cushing's syndrome of gastric erosion secondary to a cerebral lesion.

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SPECIALISM: ITS DANGERS

If the specialist in medicine is merely the physician who by long and arduous training has acquired knowledge and skill to an unusual degree, how can there be any danger? Is not specialism the very foundation of progress in the science and art of medicine, the only way by which the boundaries of knowledge can be extended? For the layman, however, dangers do exist, particularly since there is no statutory definition of specialism or the specialist, and any physician can legally apply the latter designation to himself.

What constitutes a specialty? Certainly not the mere designation of the part of the body to be treated. The qualified physician or general practitioner may treat the mind or any part of the body, no matter how many specialists claim it as their own. Yet one danger from specialism is that physician and layman may come to think that no one but a specialist is competent to practice in any field.

Another danger is that the qualified specialist may look at medicine with a microscopic eye and, of necessity, see only his chosen field, and that out of perspective. Then he may be inclined to think that the cause of all bodily ills — such as bad posture, eyestrain and indigestion — lies in his field.

But the most serious dangers arise because of the existence of the unqualified, self-designated "specialist." A little detailed knowledge may give him undue confidence so that he undertakes what is far beyond his competence. He may claim for himself what he does not possess. He may say that he is a specialist because he wants to be known as such, and because he wants to derive whatever benefit may come from such a designation. The danger at this point is substantially the danger from misrepresentation. It is not that a physician should not practice in a special field, but the claim that he is qualified when he is not.

Perhaps there should be a change in the statute, a designation there as deceit, if proper qualification for the claim to be a specialist is not shown. The difficulty then will be to determine what should be required so that a physician may properly be known and practice as a specialist. The difficulty is not insuperable, but it is clear that a man's claim for himself that he is a specialist should not be the only criterion for qualification.

SMALLPOX

Of all the communicable diseases that have scourged mankind, the one that has been immunologically preventable for the longest time and on the whole most satisfactorily is smallpox. It is a reflection on the effectiveness of our particular form of democracy, desirable as that political condition may otherwise be, that India alone has a higher smallpox rate than the United States.

Perhaps we should congratulate ourselves that the year 1939, according to a recent issue of the *Statistical Bulletin* of the Metropolitan Life Insurance Company, registered an improvement over 1938, a drop from 14,983 cases to only 10,059 — of an entirely unnecessary disease! Even with this decrease, the annual average of 9563 cases for the preceding five years is still exceeded.

The smallpox belts of the United States consist of the north-central states and those lying west of the Mississippi River — sections, apparently, where personal liberty still bulks larger, in some particulars, than does the common good. A number of these states showed a rise in smallpox incidence — notably Ohio, Indiana, Michigan, Iowa, Oklahoma and Tennessee; other records on the wrong side of the ledger were chalked up against California, Texas, Illinois and Washington. We may reasonably point with pride to the fact that the six New England states and New Jersey, Pennsylvania, Delaware and Maryland, with a combined population of over 25,000,000 have reported a total of 14 cases since 1933.

Vaccination has unfortunately been accepted for years by a vociferous group as a symbol of the loss of individual liberty. How dearly such liberty can be bought will be discovered by the north-central and western states if the present mild type of smallpox suddenly develops into the virulent variety.

MEDICAL EPONYM

Austin Flint Murmur

Austin Flint (1812–1886), then professor of the principles and practice of medicine in the Bellevue Hospital Medical College, New York City, first fully described this murmur in a paper, "On Cardiac Murmurs," which appeared in the *American Journal of the Medical Sciences* (*N.S.* **44**:29–54, 1862).

> Now in cases of considerable aortic insufficiency, the left ventricle is rapidly filled with blood flowing back from the aorta, as well as from the auricle, before the auricular contraction takes place. The distension of the ventricle is such that the mitral curtains are brought into coaptation, and when the auricular contraction takes place the mitral direct current passing between the curtains throws them into vibration and gives rise to the characteristic blubbering murmur. The physical condition is in effect analogous to contraction of the mitral orifice from an adhesion of the curtains at their sides, the latter condition, as clinical observation abundantly proves, giving rise to a mitral direct murmur of a similar character.
>
> A mitral direct murmur, then, may exist without mitral contraction and without any mitral lesions, provided there be aortic lesions involving considerable aortic regurgitation.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

Raymond S. Titus, M.D., *Secretary*
330 Dartmouth Street
Boston

Toxemia of Pregnancy, Associated with Diabetes and Resulting in Intrauterine Death

Mrs. R., a thirty-one-year-old para III with diabetes of eleven years' duration, was first seen on August 3, 1939, when she was approximately eleven weeks pregnant.

The family history was noncontributory. The patient's past history included, in addition to the diabetes, scarlet fever and measles. She had undergone a tonsillectomy and a sinus operation. Catamenia began at sixteen, were regular with a twenty-eight-day cycle and lasted two to three days. The last period began on May 13, making the expected date of confinement, February 25, 1940. The first pregnancy occurred in 1936, when the patient was delivered of a full-term, macerated fetus that was said to be "big." The second pregnancy, in 1937, ended in a spontaneous abortion at approximately ten weeks; the patient was curetted.

Physical examination on August 3 revealed a very short, stocky woman. The weight was 103 pounds, the height 4 feet, 9 inches. The heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. The blood pressure was 140 systolic, 70 diastolic. The fundus was palpable by abdominal examination. Vaginal examination revealed the cervix to be posterior, the fundus anterior.

The patient was seen continuously by her obstetrician and a specialist in diabetes. During the twenty-first week the blood-prolan level rose, and the administration of stilboesterol and Pregneninolone was begun. It remained elevated during the twenty-third, twenty-fifth, twenty-eighth, twenty-ninth, thirty-third, thirty-fourth, thirty-fifth, thirty-sixth and fortieth weeks, fluctuating between 200 and 500 rat units per 100 cc.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

On January 30 the patient entered a hospital because of blurred vision and a blood pressure of 140 systolic. On February 12 she was examined vaginally, and the cervix was found to be almost ready for induction. It was decided to induce labor the next week. On February 17 she was transferred to another hospital, and labor started spontaneously about 9:30 p.m. The membranes ruptured at 9:45 p.m. By 11:00 p.m. the cervix was fully dilated, with the head on the perineum. The head was delivered normally, the body with much difficulty. Although it was said that the fetal heart was heard five hours before delivery, the fetus was macerated. It weighed 9 pounds, 14 ounces.

A few days after delivery, the patient was transferred to the hospital she had entered on January 30, where, unfortunately, she was placed in a ward in which there was sepsis. Two days later, following a chill, the temperature rose to 103°F., the pulse to 120. A culture from the uterus showed hemolytic streptococci, and the patient was given sulfanilamide, with almost immediate marked improvement. She was discharged in good condition on March 3.

Comment. This patient was a very small woman whose normal weight was about 100 pounds. The first pregnancy illustrates the frequent phenomenon of a large child born at term in a macerated state. The second pregnancy resulted in spontaneous abortion, a complication that was frequently met with before the discovery of insulin and that still occurs. The third pregnancy progressed quite satisfactorily. Blood examination revealed a high prolan early in pregnancy, and the oral administration of stilboesterol and Pregneninolone was instituted; however, the level of the prolan was not controlled, and the patient developed definite clinical signs of toxemia — an elevated blood pressure, blurred vision, edema, and albumin in the urine. It is possible, however, that the therapy succeeded in keeping this toxemia in abeyance, because the patient was at no time clinically ill.

The patient was allowed to go nearer the end of expected confinement than she would have been a few years ago. The labor was very simple; the delivery of the head was easily accomplished, but the size of the thorax and chest made the rest of the procedure difficult. Several observers stated that they heard the fetal heart five hours before delivery, and there is also a note stating that it was audible not long before delivery; yet the fetus was born in a state of beginning maceration. It is fair to infer that if this baby had been delivered a week or ten days earlier, or had the hormonal therapy been adequate, it would have been born alive and would probably have survived, since its weight at birth was 9 pounds, 14 ounces.

Until live babies are born at term in diabetic patients suffering from toxemia that has been diagnosed by the blood-prolan level and treated by sufficient doses of estrogens and progestins, it is still a tenable dictum, so far as the infant's survival is concerned, to empty the uterus at or about the thirty-seventh week of pregnancy.

A secondary complication was the hemolytic streptococcus infection, which was undoubtedly picked up on the ward. The treatment with sulfanilamide and its rapid curative effect illustrate the value of chemotherapy in obstetrics.

COMMITTEE ON INDUSTRIAL HEALTH

Charcot Joint and Taboparesis

Viewed from an industrial standpoint the following case of syphilis is of interest.

The patient, a forty-two-year-old screw-machine operator, was a diligent, fast worker but never particularly accurate. During his period of intermittent employment from 1928 to 1940 he had had two physical examinations at the factory dispensary, both of which were essentially negative. In June, 1940, a third examination was negative except for positive Kahn and Hinton tests on blood samples.

In early July, 1940, he did not report for work and was said to be under treatment for "sciatica" by his family physician. On July 22 he appeared at the company dispensary with the following story: For the past five weeks he had been unable to work because of pain and disability of the left hip and thigh. The patient walked with a marked hip limp. Examination showed that the left thigh was 5 cm. larger than the right, and the left leg was approximately 4 cm. shorter than the right. Motions of the left hip joint were surprisingly good and appeared to be more restricted by swelling than by joint disease. The knee jerks were absent. The patient was sent to Worcester City Hospital for study and treatment. An abstract of the hospital record follows:

On admission, July 23, the patient complained of shortening in left hip and difficulty in walking of 3 weeks' duration.

For the past 3 or 4 years the patient had experienced occasional shooting knife-like pains down his legs, which he thought were due to "neuralgia." His general health had been good, and he had worked regularly. Four weeks before entry, he developed a peculiar numbness in the region of the left thigh, and he thought the part was somewhat swollen. A week later, while he was walking downtown, he suddenly, without apparent cause, developed a limp. He felt "as if something let go," and the left leg became shorter than the right. He could bear his weight, but to do so was painful at times; the limp persisted. From then on he was confined at home most of the time, and medicine furnished by his physician had given no

relief. The thigh was swollen but not especially tender; with certain positions or motions, however, he experienced acute excruciating pain in the region of the left hip joint.

Physical examination was essentially normal except for the extremities. The left thigh was regularly swollen, and there was somewhat firm, limited tenderness over the hip joint. The overlying skin was reddened, and the surface temperature seemed to be increased. The diameter of the thigh was roughly 5 cm. greater than that of the right thigh. The left leg was at least 2.5 cm. shorter

FIGURE 1.

than the right. There was fair voluntary control of the leg, but motion was limited by the swelling and underlying lesion. No knee jerks or ankle jerks were obtained; there was no Babinski sign or clonus. Sensation was preserved. A few small inguinal lymph nodes were palpable. The admission diagnoses were as follows: syphilis; gumma (?); sarcoma (??).

Urine analyses were negative. The red-cell count was 4,100,000 with 75 per cent hemoglobin, and the white-cell count 9400. The blood sugar was 90 mg. per 100 cc.; the nonprotein nitrogen, 37 mg.; the phosphatase 13.4 units; the phosphorus, 3 mg.; the calcium 8 mg. The blood Hinton and Kahn tests were positive. A clear specimen of spinal fluid contained 94 cells per cubic millimeter, of which 76 were lymphocytes and 10 polymorphonuclears; the Wassermann test was strongly positive; the gold-sol test was 5432221100; the total protein was 65 mg. per 100 cc.

On x-ray examination there was almost complete destruction of the head and neck of the left femur and some bone debris in the region of the joint (Fig. 1). There was a questionable lesion in the upper portion of the left ilium. The lesion in the left hip was thought to be consistent with a Charcot joint, but malignant tumor could not be ruled out. Re-examination was advised, and stereoscopic films showed a typical Charcot joint, with complete destruction of the head and neck of the femur and some destruction in and around the acetabulum.

The patient was irritable and troublesome at times, and euphoric and bombastic at others. A neurologist believed that the patient had taboparesis. The patient was discharged, unimproved and against advice, on August 1. The discharge diagnoses were as follows: Charcot joint, left hip; taboparesis.

The interesting features of this case are the rather sudden onset, the worker's ability to walk with a very severe hip lesion and the fact that his mental condition did not cause a falling off in his earnings up to the time of stopping work. It also shows the value of routine blood examinations of all employees.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning December 9:

BARNSTABLE

Sunday, December 15, at 4:00 p.m., at the Cape Cod Hospital, Hyannis. Obstetrical Complications with Case Histories and Clinical Problems. Instructor: John Rock. Donald E. Higgins, *Chairman.*

BRISTOL NORTH

Thursday, December 12, at 4:00 p.m., at the Morton Hospital, Taunton. Technic and Treatment of Primary, Secondary and Tertiary Syphilis. Instructor: William P. Boardman. Lester E. Butler, *Chairman.*

BRISTOL SOUTH (New Bedford Section)

Friday, December 13, at 4:00 p.m., at St. Luke's Hospital, New Bedford. Operative Obstetrics: Indications and technic. Instructor: Roy J. Heffernan. Robert H. Goodwin, *Chairman.*

ESSEX NORTH

Friday, December 13, at 4:30 p.m., at the Clover Hill Hospital, Lawrence. Therapeutic Uses of Preparations of Endocrine Glands. Instructor: Marshall N. Fulton. John Parr, *Chairman.*

ESSEX SOUTH

Tuesday, December 10, at 4:00 p.m., in the Conference Room, Salem Hospital, Salem. Recent Advances in Medical Therapeutics. Instructor: G. Philip Grabfield. J. Robert Shaughnessy, *Chairman.*

MIDDLESEX NORTH

Friday, December 13, at 5:00 p.m., at St. John's Hospital, Lowell. The Treatment of Varicose Veins. Instructor: Edward A. Edwards. William S. Lawler, *Chairman.*

PLYMOUTH

Tuesday, December 10, at 4:30 p.m., in the Nurses' Home of the Brockton Hospital, Brockton. Diagnosis and Treatment of Minor Lesions of Rectum and Anus. Instructor: Franklin G. Balch, Jr. Walter H. Pulsifer, *Chairman.*

RESOLUTION ON THE DEATH OF DR. EDMUND FRANCIS WALSH

Edmund Francis Walsh, who died on August 20, 1940, was born in 1882. He attended the Boston Latin School, where he first acquired his appreciation of literature and the classics, which later became so integral a part of his life. Following his graduation from Harvard College he began the study of medicine, receiving his degree from the Harvard Medical School in 1908. After affiliation with various Boston hospitals, he was appointed to the Medical Staff of the Boston City Hospital in 1916. Because of his studious nature and painstaking attention to exact detail, he became interested in immunology and was physician-in-chief of the Department of Immunology when he died.

Such is the framework of his life, but to these meager details much could be added by the few intimates who knew and respected him. A recluse, he, like many retiring, quiet men, led a full life among his books and in his enjoyment of the fine arts. Always kind and courteous, he will be sadly missed by his many friends; he had no enemies.

CARMI R. ALDEN, *Secretary*,
Senior Staff,
Boston City Hospital.

DEATHS

CODMAN — ERNEST A. CODMAN, M.D., of Ponkapoag, died November 23. He was in his seventy-second year.

Born in Boston, he attended St. Mark's School and Harvard College and received his degree from the Harvard Medical School in 1895. Since graduation he had practiced in Boston. He was on the staff of the Harvard Medical School from 1900 to 1915, during which time he held the positions of assistant in anatomy, assistant in clinical and operative surgery, assistant in surgery and lecturer in surgery.

Dr. Codman was a fellow of the Massachusetts Medical Society, the American Medical Association and the American College of Surgeons, which he was instrumental in founding. He also held memberships in the American Surgical Association, the American Association for the Surgery of Trauma, the Society of Clinical Surgery and the New England Surgical Society. Last January he was one of three Boston doctors to receive the gold medal of the American Academy of Orthopaedic Surgeons for his work in building a system for the exchange of specific information on cases of bone sarcoma. He was a consulting surgeon at the Massachusetts General Hospital.

His widow survives him.

HITCHCOCK — HENRY R. HITCHCOCK, M.D., of Plymouth, died November 23. He was in his eightieth year.

Dr. Hitchcock received his degree from Harvard Medical School in 1890 and had practiced in Hyde Park before going to Plymouth in 1909. He was named physician of the United States Coast Guard in Plymouth and later served on the United States Public Health Service there. Dr. Hitchcock was former assistant medical examiner for Suffolk County.

A member of the Massachusetts Medical Society and the American Medical Association, he was also a member of the Massachusetts Medico-Legal Society.

His widow and a son survive him.

MURPHY — THOMAS W. MURPHY, M.D., of Lawrence, died recently. He was in his seventy-first year.

Dr. Murphy received his degree from Tufts College Medical School in 1904 and was a retired member of the Massachusetts Medical Society and the American Medical Association.

MISCELLANY

BOSTON MEDICAL LIBRARY

VITTORIO PUTTI*
1880–1940

Putti, after a thorough medical training, became the assistant to Alessandro Codivilla, director and chief surgeon of the Instituto Ortopedico Rizzoli in Bologna. Codivilla was one of the greatest orthopedic surgeons of all time. He was the first to employ an aseptic method for skeletal traction in fractures and osteoperiosteal grafts of bone to encourage osteogenesis. It was he who first devised efficient methods for tendon transplantation and for gentle reduction of congenital dislocations of the hip. Putti worked under this master, and at his death succeeded him as the director of the institute; he was also made professor of orthopedic surgery at the University of Bologna. He was an outstanding successor. Erudite, resourceful, skilful, with extraordinary executive ability, he built up the clinic to such an extent that it has become probably the most noted bone and joint center in the world. Some years ago the Clinical Surgical Club, whose members included the most famous American surgeons, made a series of visits to all the important surgical clinics of Europe. One of the members of the club, after his return to America, said that in his estimation Professor Putti's clinic surpassed all the other clinics they saw, in organization, technic and efficiency. Putti was also chief surgeon to the Hospital for Tuberculosis at Cortina in the Dolomites and probably was responsible for its establishment.

Putti had close friends in both England and America. He had great affection for Sir Robert Jones, and before World War II was in close touch with many other English orthopedic surgeons, especially Professor Harry Platt, of Manchester. He visited this country in 1921, as guest of the American Orthopaedic Association, and for many years after that he was a frequent visitor. He delivered the Lane Lectures in California, and in 1931 was honorary chief surgeon of the Peter Bent Brigham Hospital, at Professor Harvey Cushing's invitation. In 1936 he was president of the Bologna congress of the *Societé international de Chirurgie orthopédique et Traumatologie.*

Putti contributed much to the advancement of bone and joint surgery, devising new nontraumatic methods for the early reduction of congenital dislocations of the hip, and being one of the first to report new methods and successful end results after arthroplastic operations. He originated and perfected various prosthetic apparatus in the extensive appliance shop that he established at the Instituto Rizzoli. His contributions to the literature of bone and joint surgery were valuable and many. His latest volume, *Cura operatoria delle fratture del colle del femore,* was published in Bologna in 1940.

*Books and letters and other material by and about Professor Putti are on exhibit in the rotunda of the Boston Medical Library.

About two years ago he suffered a severe attack of jaundice, from which he made a slow convalescence, but it had been believed in America that he had made a complete recovery. The exact cause of his death is unknown, but his passing has left a gap in the ranks of Italian, and indeed international, orthopedic surgeons that for the time being can hardly be filled. His legion of friends feel a sense of personal loss. His charm, his loyalty, his wisdom and his skill made him a unique character, commanding respect and compelling affection.

In addition to Putti's eminence in the field of orthopedic surgery, he gained for himself wide recognition as a medical historian. Brought up in an atmosphere of books, Putti found his greatest recreation in the history of his profession. The library in which he worked in Bologna, situated in a Benedictine monastery, known as *San Michele in Bosco,* was begun in the sixteenth century and contains manuscripts and books covering a period of over four hundred years. Not a prolific writer, he nevertheless made a distinct contribution to biography in a book entitled *Berengario da Carpi,* published in Bologna in 1937. This large quarto, handsomely printed and lavishly illustrated, contains the best account ever written of Berengario, the surgeon and pre-Vesalian anatomist who first drew anatomical figures from nature and depicted the separate muscles. Berengario taught surgery in Bologna from 1502 to 1527. In the biographical section of the book, Putti drew attention to many previously unknown editions of Berengario's works, particularly *De Fractura Caanii* (1518), which he translated into Italian as an appendix. The whole work is scholarly and could result only from profound and extensive research. Whatever claim to fame Putti may have found in his vocation, certainly his name will long be remembered for *Berengario.* He also wrote an article entitled "Historic Artificial Limbs," first published in the *American Journal of Surgery* (**6**:111–118 and 246–253, 1929) and later issued in book form (New York, 1930).

Putti was a handsome, vivacious, almost debonair person, a striking figure, both in Bologna on his orthopedic wards and in his medieval library. Both backgrounds were fitting, but we prefer to remember him in Cortina d'Ampezzo, high up in the Dolomites, one September day in 1932. Cushing, Klebs, Fulton and one of us were motoring through Italy after the Physiological Congress in Rome. We came to Cortina from Venice, crossing the Piave and going through the Fadalto Pass to Pieve di Cadore, where Titian was born. In glorious weather, the Dolomites stood out in bold relief as we entered the cup-shaped valley of Cortina. Here Putti met us, smiling, gracious and hospitable. He was justly proud of his hospital in Cortina, a "country branch" of the *Instituto Ortopedico Rizzoli* in Bologna. Facing south, in a warm valley, surrounded by green grass, with sheep nibbling in place of lawn mowers, this clean attractive hospital for patients with tuberculosis of bones and joints was obviously Putti's special pride. And well it might be, for the mahogany-brown patients, so hardened to exposure both summer and winter, that they lived out of doors practically unclothed the year around, were a living example of his skilful treatment. At a dinner that night, Putti was at his best as a genial host, but occasionally a faraway look came into his eyes, and a slight suggestion of sadness clouded his brow. Was the period of international exchange of companionship drawing to a close? Putti showed some uneasiness that night, as if his brilliant spirit were being dimmed. Parting the next day, one wondered what the future held for any of us, for we were certainly entering a new world and Putti, as well as the rest of us, was living in the past.

Unconsciously perhaps, Philippi Scaglietti, his first assistant physician in Bologna, paid to Putti the most fitting tribute, when he cabled one of us on November 1, 1940: "We are grieved to communicate the sudden death of our beloved master, Professor Putti." Master of orthopedic surgery, master of biography and bibliographic precision, Putti stands out as a towering figure, clean and straight as the Dolomites he loved so well.

H. R. V. and R. B. O.

NOTICES

ANNOUNCEMENT

Henry R. Viets, M.D., announces the removal of his office from 6 Commonwealth Avenue to 66 Commonwealth Avenue, Boston. Telephone KENmore 9430.

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, formerly concertmaster of the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will take place on Tuesday, December 10, in the amphitheater of the Peter Bent Brigham Hospital at 8:15 p.m.

Program

Presentation of cases.

The Relation of Forensic Medicine to Public Health. Dr. Thomas A. Gonzales, chief medical examiner, New York City.

NEW ENGLAND HEART ASSOCIATION

There will be a meeting of the New England Heart Association in the Moseley Building, Massachusetts General Hospital, on Monday, December 16, at 8:15 p.m.

Program

Resolution in honor of Dr. Henry Jackson, the first president of the New England Heart Association.

Mitral Stenosis after Eighty, with Especial Reference to Dr. Herman F. Vickery. Drs. Paul D. White and Edward F. Bland.

Arteriosclerotic Thoracic Aortic Aneurysms. Dr. M. deG. Ruffin. Discussion by Dr. Benjamin Castleman.

Right-Upper-Quadrant Abdominal Pain on Effort in Mitral Stenosis. Dr. Norman Boyer.

Comments on Lead 3 of the Electrocardiogram. Dr. Howard B. Sprague.

Further Experiences in the Newer Drug Therapy of Subacute Bacterial Endocarditis. Dr. C. Edward Leach. Discussion by Drs. James M. Faulkner, Charles N. Duncan, Sylvester McGinn and Saul R. Kelson.

Interested physicians and medical students are cordially invited to attend.

BOSTON MEDICAL HISTORY CLUB

There will be a meeting of the Boston Medical History Club at the Boston Medical Library, 8 Fenway, Boston, on Wednesday, December 11, at 8:15 p.m. Dr. Leonard Carmichael will speak on "Sir Charles Bell: His relation to problems of the present day."

All interested persons are cordially invited to attend.

WILLIAM HARVEY SOCIETY

The William Harvey Society of Tufts College Medical School announces the third lecture in its winter series, "The Functions of the Massachusetts Department of Mental Health, and the Preventive Program in Mental Hygiene," to be given by Dr. Clifton T. Perkins, commissioner of the Massachusetts Department of Mental Health. Dr. William Malamud, clinical professor of psychiatry at Tufts, will preside at the meeting, which will be held on Friday, December 13, at 8:00 p.m., in the auditorium of the Beth Israel Hospital. Interested members of the medical profession are cordially invited.

ARLINGTON AND BELMONT MEDICAL CLUBS

A combined meeting of the Arlington Doctors' Club and the Belmont Medical Club will be held at Ring Sanatorium and Hospital, on Tuesday, December 10, at 8:00 p.m. Dr. Chester S. Keefer will speak on "The Sulfonamide Drugs in the Treatment of Infections." A social hour will follow the program.

APPOINTMENTS IN MEDICAL CORPS, REGULAR ARMY

An examination of applicants for appointment as first lieutenants, Medical Corps, United States Army, will be held within the continental limits of the United States from March 10 to 13, 1941, inclusive. Applications and requests for information concerning this examination should be addressed to the Adjutant General, War Department, Washington, D. C. Applications received after February 20, 1941, will not be considered.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, December 8

Monday, December 9

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Tuesday, December 10

*9–10 a.m. Some Geographical Differences in Surgical Diseases. Dr. Rudolf Nissen. Joseph H. Pratt Diagnostic Hospital.

12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital amphitheater.

8 p.m. Fractional Spinal Anesthesia. Dr. M. J. Nicholson. New England Society of Anesthesiology. Massachusetts General Hospital.

8:15 p.m. Harvard Medical Society. Amphitheater, Peter Bent Brigham Hospital.

Wednesday, December 11

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital.

*8:15 p.m. Sir Charles Bell: His relation to problems of the present day. Dr. Leonard Carmichael. Boston Medical History Club. Boston Medical Library, 8 Fenway.

Thursday, December 12

*8:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Children's Hospital.

*9–10 a.m. Pathogenesis of the So-Called "Metasyphilis" (General Paresis, Tabes). Dr. Alfred Hauptmann. Joseph H. Pratt Diagnostic Hospital.

*8:15 p.m. Intraspinal Causes of Sciatica. Dr. William J. Mixter. United States Marine Hospital, Chelsea.

Friday, December 13

*9–10 a.m. Clinicopathological conference. Dr. William B. Castle. Joseph H. Pratt Diagnostic Hospital.

*8 p.m. Functions of the Massachusetts Department of Mental Health, and the Preventive Program in Mental Hygiene. Dr. Clifton T. Perkins. William Harvey Society. Auditorium, Beth Israel Hospital.

Saturday, December 14

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

December 8–11 — American Academy of Dermatology and Syphilology. Page 831, issue of November 14.

December 10 — Arlington and Belmont Medical Clubs. Notice above.

December 10 — International College of Surgeons. Page 914, issue of November 28.

December 12 — Pentucket Association of Physicians. Page 263, issue of August 15.

December 16 — New England Heart Association. Page 956.

December 27–29 — National Convention of the Association of Medical Students, Boston.

January 4, 1941 — American Board of Obstetrics and Gynecology. Page 787, issue of November 7.

March 8 — American Board of Ophthalmology. Page 201, issue of August 1.

April 21–25 — American College of Physicians. Page 1065, issue of June 20.

May 21, 22 — Massachusetts Medical Society, Boston.

June 2–6 — American Medical Association. Cleveland, Ohio.

District Medical Societies

ESSEX SOUTH

January 8 — Visceral Pain and Its Relief. Dr. James C. White. Danvers State Hospital, Hathorne.

February 5 — Subject to be announced. Lynn Hospital.

March 5 — X-ray in Heart Disease. Dr. Merrill C. Sosman. Essex Sanatorium, Middleton.

April 2 — Pediatric Problems in General Practice. Dr. Joseph Garland. Addison Gilbert Hospital, Gloucester.

May 14 — Relation of the Doctor to the Law. Mr. Leland Powers. New Ocean House, Swampscott.

FRANKLIN

January 14.

March 11.

May 13.

Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK

January 28 — Carney Hospital.

February 25 — Medico-Legal meeting. 8:30 p.m. Hotel Puritan, Boston.

March 25 — To be announced.

May 8 — Censors' meeting. Hotel Puritan.

SUFFOLK

January 29 — Page 604, issue of October 10.

April 30 — Page 604, issue of October 10.

WORCESTER

December 11 — St. Vincent Hospital, Worcester.

January 8, 1941 — Worcester City Hospital, Worcester.

February 12 — Worcester State Hospital, Worcester.

March 12 — Memorial Hospital, Worcester.

April 9 — Hahnemann Hospital, Worcester.

Supper at 6:30 p.m. followed by a business meeting and scientific program.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in

regard to all listed books will be gladly furnished on request.

Clinical Urology. By Oswald Swinney Lowsley, A.B., M.D., director of the Department of Urology (James Buchanan Brady Foundation), New York Hospital, and Thomas Joseph Kirwin, M.A., M.S., M.D., attending surgeon, Department of Urology (James Buchanan Brady Foundation), New York Hospital. 8°, cloth; Vol. 1, 898 pp., with 220 illustrations; Vol. 2, 785 pp., with 145 illustrations, 7 plates and 9 tables. Baltimore: Williams & Wilkins Company, 1940. $10.00 for the set.

Rose and Carless Manual of Surgery. American (sixteenth) edition. Edited by William T. Coughlin, B.S., M.D., professor of surgery and director of the Department of Surgery, St. Louis University School of Medicine; surgeon-in-chief, St. Mary's group of hospitals, St. Louis, Missouri. From the sixteenth English edition by Cecil P. G. Wakeley, D.Sc., F.R.C.S., F.R.S.E., F.R.S.A., F.R.A.C.S., fellow of King's College, London, senior surgeon, King's College Hospital; director of surgical studies and lecturer in surgery, King's College Hospital Medical School; surgeon, Belgrave Hospital for Children, and West End Hospital for Nervous Diseases; consulting surgeon, Maudsley Hospital and to the Royal Navy; Hunterian Professor, Royal College of Surgeons of England, and John B. Hunter, M.C., M.Chir. (Cantab.), F.R.C.S. (Eng.), surgeon, King's College Hospital; lecturer in surgery, King's College Hospital Medical School; surgeon, Royal Chest Hospital; consulting general surgeon, Throat, Nose and Ear Hospital, Golden Square. 8°, cloth, 1656 pp., with 1034 illustrations and 30 colored plates. Baltimore: Williams & Wilkins Company, 1940. $9.00.

A Manual of Embryology: The development of the human body. By J. Ernest Frazer, D.Sc. (Lond.), F.R.C.S. (Eng.), professor of anatomy in the University of London. Second edition. 8°, cloth, 523 pp., with 282 illustrations. Baltimore: Williams & Wilkins Company, 1940. $9.00.

Surgery of the Hand. By R. M. Handfield-Jones, M.C., M.S., F.R.C.S., surgeon to outpatients, St. Mary's Hospital; senior surgeon, Florence Nightingale Hospital; consulting general surgeon, Hospital for Women, Soho Square; consulting surgeon to the London County Council; lecturer in operative surgery, St. Mary's Hospital Medical School; late Hunterian Professor, R.C.S. 8°, cloth, 140 pp., with 95 illustrations. Baltimore: Williams & Wilkins Company, 1940. $4.50.

The Control of Tuberculosis in the United States. By Philip P. Jacobs, Ph.D., director of personnel training and publications, National Tuberculosis Association. Revised edition. 8°, cloth, 387 pp. New York: National Tuberculosis Association, 1940. $2.00.

History of Pharmacy: A guide and a survey. By Edward Kremers, Ph.G., Ph.M., Ph.D., ScD., former professor of pharmaceutical chemistry, University of Wisconsin, and George Urdang, Ph.G., D.Sc.Nat. 8°, cloth, 466 pp., with 30 illustrations. Philadelphia: J. B. Lippincott Company, 1940. $4.50.

BOOK REVIEWS

The Diagnosis and Treatment of Cardiovascular Disease. Edited by William D. Stroud, B.S., M.D. Volume I, 4°, cloth, 832 pp., with 163 illustrations. Volume II, 4°, cloth, 855 pp., with 153 illustrations. Philadelphia: F. A. Davis Company, 1940. $18.00.

These two large volumes, handsomely bound and copiously illustrated, consist of sixty-two chapters that range from the classification of cardiovascular diseases through congenital, rheumatic and other types of heart disease to electrocardiography, roentgenology, dysfunction, medical and surgical treatment, public-health problems and vascular anomalies. The work is an amplification of the section, "The Diagnosis and Treatment of Cardiovascular Disease," also edited by Dr. Stroud, and included in the *Encyclopedia of Medicine,* first published by the F. A. Davis Company in 1934.

The fifty-six contributors include many specialists in the field throughout the country. As is true of any such encyclopedic work, the quality of both the subject matter and the prose style varies considerably. However, the great bulk of the work is reliable and up to date, and these volumes, although not intended for the library of the general practitioner, should be useful as reference works in medical libraries, hospitals, medical schools and medical centers.

American Doctors of Destiny: A collection of historical narratives of the lives of great American physicians and surgeons whose service to the nation and the world has transcended the scope of their profession. By Frank J. Jirka, M.D., with an introduction by Harold W. Camp. 8°, cloth, 361 pp., with 20 portraits by Raymond Warren. Chicago: Normandie House, 1940. $3.75.

Dr. Jirka has written an interesting, if somewhat unusual, history of American medicine. The book is built around his "doctors of destiny," one chapter being devoted to each character. The list sets the general tone of the book. With Shippen, Warren, Rush, McDowell, Drake, Morton, Holmes, Reed, Gorgas and possibly Weir Mitchell, Leonard Wood and W. W. Mayo as the chief candidates, most historians would agree. One misses Waterhouse, Hosack, Physick and a number of others. Jirka adds Henry Dearborn, Samuel A. Mudd, Charles Norris, Franklin H. Martin, Leo L. Stanley, James S. Greene and Frederick Tice, some of whom are almost unknown and are of such slight importance that their inclusion is hardly justifiable. His loyal Chicago associations have served to unbalance an otherwise well-conceived book. There is a final chapter, with a portrait, on the work of Frank J. Jirka, the author. The book is only slightly documented, and some statements are open to question. There are many other books covering the same ground that are far superior to Dr. Jirka's efforts as a medical historian. A series of twenty portraits, painted for this book, do not add to its value.

Manual of Dermatology. By Carroll S. Wright, B.S., M.D. 8°, cloth, 376 pp., with 138 illustrations. Philadelphia: Blakiston Company, 1940. $4.00.

This manual was written chiefly for medical students and general practitioners. It is useful as a ready reference book since the average textbook in dermatology is too voluminous to be practical. The method of presentation corresponds with the previously published compend, *Diseases of the Skin,* by Jay F. Schamberg, with some reclassification of the text and many new photographs added. The volume can be recommended as a practical, compact volume to be amplified by the larger textbooks for those who wish more complete subject matter and bibliography.